University of Southern Queensland

Faculty of Engineering and Surveying

Investigation into the Non-Invasive Monitoring of Blood Glucose Levels in People with Diabetes

A dissertation submitted by

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Abstract

Diabetes Mellitus is a condition that reduces the body's ability to maintain normal blood glucose levels. Maintaining the correct blood glucose level is important as it provides different parts of the body with energy to function properly. Because of this, diabetics must be able to know what the levels are, so they can control them with supplements or other treatments.

At present, people with diabetes must monitor their blood glucose levels using invasive techniques like needles and pin-prick devices sometimes up to three or four times a day, depending on the severity of their condition. Because of the pain and inconvenience of testing using this method, sufferers don't always test themselves as often as they should.

A non-invasive, *in vivo* system of monitoring blood glucose levels is the vision of this investigation. Being non-invasive would make the task of measuring blood sugar painless. *In vivo,* in a clinical testing sense means constantly monitoring. This is in contrast to the *in vitro* method commonly used today where blood is extracted with the needle or pin-prick and analysed. As much a problem as pain for the diabetic is the inconvenience of having to stop what they are doing and test themselves. A solution could be a device which constantly monitors without being prompted by the user. An *in vivo* system has advantages as it could be used in the future to provide a closed-loop insulin delivery system (i.e an artificial pancreas), and it can provide alarms for hypoglycaemic (low glucose) and hyperglycaemic (too much glucose) attacks.

There have been some studies into using near-infrared light to measure the glucose levels, but as yet this method is not accurate enough for clinical applications. This project will investigate the method and determine if there are any ways to improve the quality of signals or similar alternatives.

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Ross Donald Gillies

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R. Gillies

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Chapter 1 : INTRODUCTION

1.1 Introduction

This chapter gives a brief overview of what is covered in the dissertation. It contains the project aims, as formally recognised in the project specification, and also provides a brief summary of all the chapters of this document.

1.2 Project Aims:

There are a numbers of goals I have set for this project. The basic plan was set out in the project specification (last ed. 24th May, Appendix A: PROJECT SPECIFICATION).

1. Research briefly the diabetic condition.
2. Research the different types of medical sensors available at present, if they exist what they are able to measure and the format of their output.
3. Perform testing on glucose solutions (possibly in the body) and measure the output signal.
4. Construct empirical models of blood glucose based on the testing.
5. If time permits, I would like to design control systems based on the empirical models that may be later implemented on a PC or on an embedded system.

Not all of these goals were achieved, due to the development of circuits taking longer than I had expected and the lack of positive results from testing. The research that was done is summarised in the dissertation overview.

1.3 Dissertation Overview

Chapter 2: DIABETES

This chapter will explain the condition Diabetes Mellitus in basic medical terms, the effects of the disease on the body, and present treatments. Statistics on the extent of the disease in Australia, and in particular the Aboriginal population are given.

Chapter 3: EXISTING GLUCOSE SENSORS / TECHNOLOGIES

There are a number of different glucose sensors in present use and development which have been researched, and are reported in this chapter.

Chapter 4: USING LIGHT FOR MEASUREMENT

This project has focussed on the use of light for analysis of test substances; in particular light in the near-infrared range is dealt with. Included in this chapter are details of some experimental work done on measuring light absorbance and reflectance to analyse samples.

Chapter 5: CONCEPTUAL SYSTEM DESIGNS

The conceptual designs in this chapter are aimed at analysing a test sample using infrared light and communicating the results through various interfaces to the diabetic or their carer. Two main systems with microcontrollers are designed, one using a PIC and the other using a Motorola.

Chapter 6: BASIC SENSOR CIRCUIT DESIGN

Before anything as elaborate as the systems designed in chapter five are built, it would be important to know if the basic sensor circuits are actually capable of measuring glucose. This chapter looks at what components are available for producing and measuring light, and details the design of a circuit to use in testing.

Chapter 7: TESTING FOR GLUCOSE

Using the circuit developed in Chapter 6, tests were carried out by varying the concentration of a glucose solution. The methods, results and brief discussion are presented in this chapter.

Chapter 8: CONCLUSIONS AND RECOMMENDATIONS

This chapter summarises the project, its content and value. The results of testing are explained in the context of the whole project. The chapter will all recommend some further work for research in the area of non-invasive blood glucose monitoring.

Chapter 2 : DIABETES

2.1 Introduction

Diabetes is a condition which affects the body's ability to maintain normal blood glucose levels. It is caused by resistance to, or deficient production of the hormone insulin, which helps to move glucose into the cells. When the body does not produce or use enough insulin, the cells cannot use glucose and the blood glucose level rises. When the body cannot use glucose it starts converting body fat and muscle to energy. The disease leads to problems with the heart, kidneys, blood vessels, nerves and eyes. (Australian Government, 2003)

Diabetes is dependent on carbohydrate metabolism, or the body's ability to use carbohydrates, in particular the simple sugar, glucose. Diagnosis of the disease is mostly based on glucose measurements in blood and urine samples or the tolerance of an individual to an extra load of glucose; and treatment is usually in the form of glucose or other sugar supplements.

There are three main types of diabetes: Juvenile-onset (type I) or insulin-dependant diabetes mellitus (IDDM); adult-onset (type II) or non-insulin dependant diabetes (NIDDM); and gestational diabetes. These three conditions account for over 98% of all diabetes. Other forms include Diabetes Insipidus, where the kidneys are unable to conserve water, resulting in frequent urination.

Type I diabetes, in most cases will develop in people before the age of 18 years. In type-1 diabetes, the body destroys its insulin creating cells in the pancreas, so that children with this disease need to frequently inject themselves with insulin supplements.

Type II diabetes is most prevalent in older people, and increasingly in younger people and can in part be caused by the person by their eating habits, or as is more likely the case in the elderly a sedentary lifestyle. It is mostly genetic in origin, but factors such as increasing age, excess weight, inactivity, high blood pressure and poor diet all contribute to increasing a person's risk

of the disease. The condition affects the body's ability to maintain normal blood glucose levels. It is caused by resistance to, or deficient production of, the hormone insulin, which helps glucose move from the blood into the cells. Many people with the disease do not even know they are suffering from it. The consequences of not being diagnosed and treated are an increased risk of coronary heart disease and kidney disease. In its initial stages, the condition can be managed through careful exercise and dietary programs and oral drugs, but if it develops to a more serious level, the sufferer may require insulin injections.

2.2 Other Effects of Diabetes

Diabetes also has other affects on the body. Diabetic retinopathy is a disorder affecting the blood vessels in the eye. It involves the growth of abnormal new blood vessels in the eye which can impair vision, and also the occurrence of blood clots and haemorrhaging of blood vessels in the retina. The condition can cause retinal detachment, cataract formation, and maculopathy, which all lead to forms of blindness. It is possible, that diabetes monitoring could be done with eyes as a basis. The most important point to make here though is that blindness or partial blindness can be more common in diabetes sufferers so any monitoring device should be designed accordingly. If sufferers need to rely on a visual readout of blood glucose levels, a monitor may not be of use. Presently on the market is a device called the 'talking' blood glucose meter, which as the name suggests gives an audio report of its measurement.

Juvenile-onset diabetes can commonly cause hypoglycaemic attacks. These attacks, where the sufferer has dangerously low levels of glucose in the blood has been linked to neurologic sequelae, or damage to the nervous system.

At present, most diabetes sufferers need to monitor their blood glucose levels several times a day. Home glucose monitoring requires the sufferer to draw a drop of blood, usually from the fingers and place it on a small window in a test strip. The glucose causes a chemical reaction with the test strip, producing light, which can be detected using a reflectance meter.

The obvious disadvantage of this system is that the sufferer needs to draw blood from themselves. As well as pain, the process can cause calluses and increases risk of warts and infections. It would be a great relief for them then if some form of non-invasive monitoring device could be developed.

2.3 Major Diabetes Statistics

According to the Australian Institute of Health and Welfare, Diabetes accounted for 5% of the total financial burden of disease in Australia. In 2002, 8% of all deaths in Australia reported diabetes as the underlying or associated cause of death. A survey of 3% of Australia's general medical practitioners found that diabetes was the sixth most common problem managed. In 2003, more than 86,000 Australians had some disability caused by diabetes.

Type I diabetes accounts for 10-15% of all diabetes cases. Based on figures from the Australian Bureau of Statistics, 95000 people in 1997 were suffering from the disease, and more than 98% of these were children.

More than 85% of diabetes cases are type II. It was estimated in 1999 by the Australian Diabetes, Obesity and Lifestyle Study that 7% of Australians suffer from this disease (900,000 people). But it was also estimated that 50% of the people living with the disease do not know that they have it. (Dixon, T, 2005)

2.4 Diabetes in Indigenous Australians

Due to the lifestyles that western cultures allowed the Indigenous Australians to live (introducing them to alcohol, different foods, and less active lives), the earlier part of the 20th century saw a relatively high incidence of type II diabetes in the Indigenous population. A report titled *"The Katherine Region Diabetic Retinopathy Study"* looks at the way the lifestyle change caused by the introduction of western culture affected the occurrence of diabetes in indigenous people in that area, particularly with respect to diabetes-based retinopathy (see section 1.1 for definition). Based on figures in the 1989-1990 and surveys of people with and without diabetes, it was estimated that the occurrence of diabetes was 2 to 4 times greater than the whole population, depending on different Indigenous communities. Diabetes in the whole population of Australia was estimated to be around 6% (based on commonly used assumption that only 50% of sufferers are aware of the condition, and that 3% of the population were actually diagnosed with the disease). (Jaross, N; Ryan, P; Newland, H, 2003)

2.5 Treatment of Diabetes

The treatment of diabetes is a day to day self-management. A diabetic must monitor their glucose levels regularly and take appropriate action, make significant lifestyle changes, consult

regularly with health-care professionals, take appropriate medications and be emotionally stable.

The most common form of diabetes, type II can be prevented, or controlled to some extent with a healthy lifestyle, which means enjoying healthy easting, maintaining a healthy weight, and being physically active. Healthy eating involves developing a plan to control glucose intake, lower cholesterol, and improve overall health. In particular, meals should include at least one food with low Glycemic Index (G.I) such as grainy bread, cereals and some fruits to balance blood glucose levels. These low G.I. foods provide a steady release of glucose into the blood, as they contain more complex carbohydrates, which take longer to digest. For a healthy diet, diabetics in particular but also all other people should limit the amount of medium to high G.I. foods, like those that contain large amounts of sucrose or table sugar and glucose, as these foods can rapidly change the glucose levels in the blood.

In type I diabetes and more severe cases of type II diabetes, controlling diet and exercise are not enough to control blood glucose levels; medications must be taken. Insulin hormone supplements are commonly used, especially for type I diabetes where the body's own immune system targets and destroys the insulin-producing cells in the pancreas. A sign that the insulin levels are too low is a high level of glucose in the blood, since the function of insulin is to control and excrete (remove from the body) surplus glucose. In the case of a hypoglycaemic attack where the blood glucose level falls dangerously low, as can happen after skipping a meal or doing excessive exercise, the treatment is in the form of glucose tablets or jellybeans. (International Diabetes Institute, 2005)

2.6 Type II Diabetes Predisposition

Type-II diabetes or NIDDM is considered to be preceded by cycles of insulin resistance and hyperinsulinemia (too much insulin). This is sometimes referred to as "metabolic syndrome". An article published by the International Society for Optical Engineering in 2002 discusses the use of mid-infrared spectroscopy on dried serum specimens.

The spectroscopy was applied to small samples (1µL) from six donors and evaluated using disease pattern recognition (DPR). Substantial differences in spectra were found between healthy subjects and those with the metabolic syndrome.

2.7 Glucose

2.7.1 Glucose Molecule

Glucose is one of at least three simple sugars to share the same molecular composition; that is $C_6H_{12}0_6$ or 6 carbon atoms, 12 hydrogen atoms and 6 oxygen atoms. The structure is shown in Figure 2-1.

Other simple sugars with the same composition but different structure are fructose and galactose. The molecular masses of the components are:

M_{Carbon} = 12.0111 g/mol; $M_{Hydtogen}$ = 1.0079 g/mol; M_{Oxygen} = 15.9994 g/mol

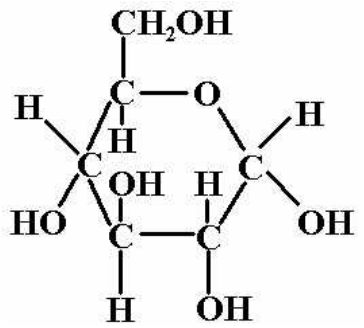

Figure 2-1 Glucose Molecule

This means that the molecular mass of glucose is:

$$M_{Glucose} = 6\times 12.0111 + 12\times 1.0079 + 6\times 15.9994$$
$$= 180.158\ g$$

.....EQ. 2-1

2.7.2 Units of Measurement

The SI (Systemme International) units to describe glucose concentration are mmol/L (milli-moles per litre). Another common unit used though is mg/dL (milli-gram per deci-litre). This is used mostly in the US. One mole is $6.23x10^{23}$ molecules. The weight of one mole glucose is 180.158 grams, so the conversion from mmol/L to mg/dL is:

1mmol/L = 18.016 mg/dL

This becomes important when gathering information from different sources.

2.7.3 Typical Glucose Levels and What They Indicate

Table 2-1 gives a rough indication of what levels of glucose in the human body mean. The boundaries of classification increase as concentration increases, which may mean that a sensor should take a logarithmic measurement rather than linear. The table is only a rough chart, and would need to be calibrated to individuals by a health-care professional. For classification of a person's health, a home-test meter should only allow 15% error.

Table 2-1 - Interpretation of glucose levels in the blood

Concentration of glucose (mmol/l)	Concentration of glucose (mg/dl)	Medical interpretation
2.0	35	Extremely low, danger of unconsciousness, hypoglycaemia
3.0	55	Low, marginal insulin reaction
4.0	75	Slightly low, first symptoms of lethargy etc.
5.5	100	Accepted healthy level of blood glucose
5-6	90-110	Normal healthy levels of glucose before meals in non-diabetics
8.0	150	Normal healthy levels of glucose just after a meal in non-diabetics
10.0	180	Maximum healthy levels of glucose just after a meal in non-diabetics
11.0	200	
15.0	270	A little high to very high depending on patient – factors include severity of condition, time of last meal, age, weight
16.5	300	
10.0	360	Getting up there
22	400	Maximum concentrations for some meters and strips
33	600	High danger of severe electrolyte imbalance, hyperglycaemia

2.8 Conclusion

This chapter has explained briefly the disease Diabetes Mellitus, its effects and how it is managed / treated, and the justification of the research project. The statistics show how large

the issue of diabetes is at present and what it is expected to be in the future of Australia's population. The need to be able to monitor blood glucose is real in diabetics, and any way that makes the monitoring of levels more comfortable for the diabetic is obviously important. The next chapter introduces some of the sensor technologies used at present for monitoring blood glucose levels.

Chapter 3 : EXISTING GLUCOSE SENSORS / TECHNOLOGIES

3.1 Introduction

In diabetes sensors both in vivo and in vitro sensors in the usable and experimental stages exist. *In vitro* sensors include dry reagent strips, reflectance meters, which are used in the home, and large automatic glucose analysers in the hospitals and clinical laboratories. *In vivo* sensors are mostly experimental at the moment, but they will be of great assistance to diabetic patients, to warn them of hypoglycaemia, hyperglycaemia, and to monitor glucose levels during surgical procedures.

3.2 Types of Sensors

In vivo sensors can be separated into two categories: invasive and non-invasive.

Invasive Sensors

- Enzyme electrodes
  - Amperometric (non-mediated)
    - H_2O_2 – detecting
    - O_2 – detecting
  - Amperometric (mediated, ferrocene-based)
  - Potentiometric, e.g., field effect transistor
- Optical sensors
  - Bioaffinity probe
  - Glucose-oxidase based
- Microdialysis systems

Non-Invasive Sensors

- Near infra-red spectroscopy
- Near Infrared Diffuse-Reflectance Spectroscopy
- Photo-acoustic spectroscopy
- Light scattering
- Reverse iontophoresis
- Thermal emission spectroscopy
- Raman Spectroscopy

(John C. Pickup, 1997)

3.3 Invasive Sensors

Most of the research on *in vivo* sensors has been with implantable systems, particularly the amperometric enzyme sensors.

3.3.1 Enzyme Electrodes

Enzyme electrodes are used to catalyse chemical reactions and various transducers are used to detect the reactions that occur. A commonly used enzyme is glucose oxidase, which induces a reaction between glucose and oxygen to produce gluconic acid and hydrogen peroxide. This peroxide breaks down to oxygen and hydrogen and eventually turns into water. In doing so, it produces a voltage which can be measured by electrodes. Commonly, these types of sensors will take over 60 seconds to get a reading, because the time needed for the reaction to take place.

Electrodes are mostly implanted into the sub-cutaneous (just under the skin) layer, because implantation into the blood stream could result in coagulation of blood, leading to thrombosis (blood clots), and the risk of infection. In the sub-cutaneous layer, the sensors are in contact with interstitial fluid. It is assumed that this interstitial fluid has a similar concentration of glucose as the blood, and experimental results support the assumption. Actually sensor-recorded sub-cutaneous glucose levels have been found to be usually between 20 and 90% of simultaneously recorded blood glucose levels. This error margin is attributed to the electrodes rather than the physiological composition.

Potentiometric sensors contain special field effect transistors in their electrodes which output a current proportional to the pH of a contacting solution.

There is substantial research in the area of enzyme electrodes, and it is one of the most likely candidates for use in a closed-loop insulin delivery system.

3.4 Non – Invasive Sensors

3.4.1 Near-infrared (NIR) Spectroscopy

NIR is defined as light in the spectrum range of between 700 and 1000nm. At this wavelength, light can pass through several centimetres of tissue. The main difficulties with this technique are the large absorption values of water, and the similar absorption behaviour of proteins and non-glucose metabolites. Multivariate statistical analysis over the full range of the useful NIR spectrum can be used to derive the glucose levels.

3.4.2 Near Infrared Diffuse-Reflectance Spectroscopy

A journal article published by the Society for Applied Spectroscopy details the use of a pair of source and detector optical fibres on the forearm for *in vivo* experiments in measuring glucose levels. Unfortunately only the abstract is available, it would be a very interesting article to read.

The optical fibres are separated by 0.65mm (the distance is based on the skin's optical properties) on the skin surface of the forearm of test subjects. Tests were carried out on six subjects, including one with type I diabetes, with encouraging results. The tests involved subjects orally taking glucose, and measuring the NIR skin spectra at the forearm. Partial least-squares regression analysis was carried out on the values obtained. Separate calibration models were used for each person in the tests, though the regression coefficients of the calibrations were similar to each subject. The characteristic absorption peak of glucose (1600nm) was confirmed by a peak in the results.

There are other sources which discuss a similar glucose test method, where some devices are inserted into the skin.

3.4.3 Photo-acoustic Spectroscopy

This technique involves sending a pulsed NIR signal into the tissues and measuring resulting ultrasound waves. As the NIR is projected through the tissue, it will cause local thermal expansion of molecules such as glucose, which in turn causes a vibration and hence sound. The signal is then detectable at the skin surface by a piezoelectric microphone.

3.4.4 Light Scattering

The refractive index of a solution, for example blood, is affected by the blood glucose levels. As glucose level increases, the scattering coefficient of light decreases, and this can be measured.

3.4.5 Reverse Iontophoresis

To explain what is meant by the term, there is a product which already uses the technique with some degree of success, aptly named the “GlucoWatch”. The GlucoWatch G2 is a non-invasive glucose monitor which is capable of continuous monitoring. It is based on the non-invasive extraction of interstitial fluid from the skin. Results obtained from trials of the device suggest that it is more effective than skin puncture sampling for optimal therapy of children suffering from type I or juvenile diabetes, mostly because it is more comfortable to wear. The device is not as accurate as tried skin puncture techniques however, and is only really good for high levels of glucose concentration. When it comes to detecting hypoglycaemic attacks, a problem mostly for type I diabetes sufferers where the glucose levels are less than what is needed for correct bodily function, the GlucoWatch is not as useful. Below about 100mg/dL, the device is inaccurate.

Extraction of interstitial fluid works by a process called iontophoresis. In this process, a low-level electric current is passed through the skin and by electro-osmosis, neutral molecules are secreted in an induced solvent flow.

The GlucoWatch device was used in a trial to measure blood glucose six times for each hour of testing. The basic aim of the device is to alert the wearer of hypoglycaemic (less than optimal range blood glucose) or hyperglycaemic (greater than optimal range) conditions. Without the availability of constant intravenous glucose measurement (via pin-prick or similar tests), the result accuracy can be somewhat questionable, coupled with the effects of perspiration and other bodily secretions. Long term studies also need to be carried out on the effect of iontophoresis on the microvascular system (smaller blood vessels). Documented testing by the

Jaeb Center for Health Research, in Tampa, Florida found that the results from the GlucoWatch were not very accurate, only 31% of results falling within 15 mg/dL of the reference, or trusted accurate result. If you consider the range that glucose concentration varies over (between 100 and 180 mg/dL is considered healthy), 15mg/dL is a significant difference. Basically, if used periodically, the GlucoWatch can be used as an indicator of trends in the body's glucose levels, but not to discern actual levels. Thus, the GlucoWatch must be used in conjunction with other test equipment.

3.4.6 Thermal Emission Spectroscopy

Thermal emission from glucose (among other substances) can be detected using room temperature detectors in a filter-based setup. In this technique, glucose is measured using the thermal emissions (radiation in the mid-infrared range). A company called Infratec has developed a device which is capable of detecting serum glucose. An independent study on the device has shown that the device demonstrates a reasonable accuracy of measurement, with the mean absolute relative error at 11.6%. (Buchert, J, 2004).

3.4.7 Raman Spectroscopy

Raman spectroscopy is being trialled in the measurement of glucose concentrations in the aqueous humor of the eye. The Raman Effect was discovered in 1928 by an Indian physicist. It is based on the way that photons (packets of light-energy) interact with molecules. A relatively high percentage of light will conform to the Rayleigh Effect where the molecules react elastically to photons and will bounce the light back at the same frequency. The Raman effect happens in about one in 10^7 photons, where the molecule does not react elastically, but scatters the incident light at a lower energy (and therefore different frequency). Devices measure this amount of scattered light, and can relate the frequency and intensity of it to characteristic values glucose concentrations (or whatever they are designed to look for).

Using this particular technique, it is possible to individually identify every metabolite in the aqueous humor of the eye, including glucose. It is relatively inexpensive, though there is a problem with noise in the signal. A fourth-order filter, called the Savitzky-Golay can be used to smooth the signal in software. (Goetz, M; Cote G; Motamedi, M, 1994), (Ergin, A; Vilaboy, M; Tchouassi, A; Greene, R; Thomas, G, 2003)

3.4.8 Hologram Sensors

Current developments in holographic contact lenses by SMART Holograms could actually provide the answer to low-cost, non-invasive blood sugar monitoring. As much as could be obtained from the SMART website was that the basic principle involved some kind of chemical reaction to body fluid that produced a characteristic change in the light properties of the lens. This change in light properties can be monitored continually. The contact lens then potentially benefits the wearer in more than one way, as diabetes is a common cause of partial blindness. SMART has a patent on these lenses already and plans to launch them commercially in the near future.

The research behind this use of holographic lenses was conducted by the Institute of Biotechnology at the University of Cambridge. Inside the lenses is a matrix containing phenylboronic acid derivatives. The acid reacts with sugars in the bodily fluids at the eye (i.e. tears), causing the cells (hydrogels) of the matrix to expand and this in turn causes a "red-shift" or increase in light wavelength in the lens. Though the acid is not selective on what sugars it reacts with, fortunately glucose has the highest concentration of blood sugars. Lactate reacts more readily with the acid, but different types of phenylboronic hydrogels used together increases the overall selectivity of the lens.

This is approaching the task of glucose detection from a different angle to the focus of this project (i.e. near-infrared spectroscopy), but essentially it has reached the same aims. It is a relatively inexpensive (only assumed, as SMART has not released the lenses but has said they are easy to manufacture) non-invasive and potentially in vivo (acid matrix responds dynamically to sugars) technique of measuring glucose concentration.

3.5 Conclusion

This chapter has given a brief introduction to the various sensors both in development and present use, including some that are non-invasive. Although the project focuses on the use of light absorbance measurements to determine glucose levels, there are a range of different indicators of glucose levels. These indicators include:

- Chemical reaction of glucose with a specific enzyme to produce an electromagnetic potential (enzyme electrodes);
- Response from exciting glucose with a near–infrared light impulse in the form of measurable vibrations (photo-acoustic spectroscopy);
- Composition of interstitial fluids (reverse iontophoresis);

- Thermal (mid-infrared light) emissions from the blood;
- Chemical reaction of sugars in the tears with phenyl-boronic acid (used in "SMART Hologram" lenses).

The next chapter will expand on the use of light for measurement of blood glucose levels.

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Chapter 4 : USING LIGHT FOR MEASUREMENT

4.1 Introduction

Absorbance and reflectance of light is used in many applications to determine the contents of a sample, from quality control in the food industry to pathology. This chapter focuses on the use of near-infrared light to measure blood glucose, but also looks at pulse-oximeters; light measuring devices for detecting oxygen levels in the blood. The first section summarises an experiment performed by a team of researchers at a Chinese University to determine the accuracy of glucose sensors. Other sections discuss some of the methods of measuring light, and the final section why the near-infrared range is used in clinical applications.

4.2 Fundamental Study on Non-invasive Blood Glucose Sensing

This section briefly describes an experiment conducted by researchers at Tianjin University in China (Maruo K, Tsurugi M, Tamura M, Ozaki Y, 2003) to create a model for signal calibration of a near infrared glucose sensor. Spectroscopic analysis of blood for glucose and other components is theoretically possible and tests have been done. Results of the tests indicate that position of measurement sensors on the human body is an important factor. Once a device has been designed in this project, the methods of testing will be similar to this experiment.

4.2.1 A model for prediction accuracy analysis:

For this type of spectroscopic analysis, the amount of light absorbed is what we want to know. But the quantity that is actually being measured is the difference between transmitted and

incident light intensity (refer to Chapter 6 for how light intensity can be measured). The model that is proposed by the research at Tianjin University is given in equations 4-1 to 4-6, where it is assumed that the ratio of transmitted light and incident light is a function of the absorptivity of the test material / substance, the concentration of the absorbent, and the length of the light path between transmitter and receiver. Furthermore, the absorptivity of the test substance is a function of the wavelength of the light transmitted. In the testing and calibration stages, the length of the light path, amount of light transmitted and concentration of the test substance could be controlled. It is then a matter of measuring the amount of incident light for a variety of concentrations, to determine whether there is a distinct correlation between concentration of test substance and light intensity for a given wavelength of light. The testing phase of this project tries to accomplish this by varying the concentration of glucose in water, for LEDs with different peak wavelengths. Testing is reported in Chapter 7.

$$I = I_0 e^{\left(-\sum_{i=1}^{n} a_i(\lambda) c_i L\right)} \quad \text{.....EQ. 4-1}$$

$$dI_s = I_0 e^{\left(-\sum_{i=1}^{n} a_i(\lambda) c_i L\right)} \left(-\sum_{i=1}^{n} a_i \frac{dc_i}{dc_j} L\right) c_j \quad \text{.....EQ. 4-2}$$

Where I = intensity of transmission light;

I_0 = intensity of incident light;

n = number of components in solution;

α_i = absorptivity;

λ = wavelength of light transmitted;

c_i = concentration of absorbent;

L = length of light path;

dI_s = change in signal light intensity;

c_j = concentration to be predicted;

It is assumed that there is no correlation between the different components. In terms of equation 4-2, this means that if the concentration of the absorbent, c_i, is different to the concentration of the component to be predicted, c_j, there is no rate of change of concentration of absorbent with respect to the concentration to be predicted:

$$if\ i = j,\ \frac{dc_i}{dc_j} = 1;$$

$$dI_s = I_0 e^{\left(-\sum_{i=1}^{n} a_i(\lambda)c_i L\right)}\left(-\sum_{i=1}^{n} a_i L\right)c_j \quad \text{.....EQ. 4-3}$$

$$if\ i \neq j,\ \frac{dc_i}{dc_j} = 0;$$

$$\therefore\ dI_s = 0$$

And,

$$dI_N = \frac{I}{SNR} \quad \text{.....EQ. 4-4}$$

Where dI_N is the change instrument noise, and SNR is the signal to noise ratio.

Now if $dI_N = dI_S$, dc = minimum change in concentration (dc_{im})

$$\left|dc_{im}\right| = \frac{1}{\alpha_i(\lambda).L.SNR} \quad \text{.....EQ. 4-5}$$

Equation 4-5 implies that when a signal to noise relationship is determined from testing, we have a limit for the observed change in concentration of a sample. The signal to noise ratio will be dependent on the electrical losses in any test circuitry, as well as the noise produced by background radiation, and other factors within the body. If this model is valid, then it is very important. The signal to noise ratio would need to be increased enough to at least achieve the home-test accuracy of ±15% of glucose levels (a low as 0.15 mmol/L in the blood).

4.2.2 Prediction Accuracy (using Partial Least Squares):

The Root Mean Squared Error of Prediction (equation 4-6) is a model that was used in the Tianjin study to set control limits on the error in predictions. If the research for this project was to get to that stage, a similar model could be used.

$$RMSEP = \sqrt{\left\langle \sigma^2, B^2 \right\rangle} \quad \text{.....EQ. 4-6}$$

Where σ = standard deviation, at each λ

B = regression co-efficient

$\sigma^2 = [\sigma_1^2, \sigma_2^2, \sigma_3^2, \ldots]$

$B^2 = [b_1^2, b_2^2, b_3^2, \ldots]$

4.2.3 Experiment Methods

In the experiment by the Tianjin researchers, the prediction accuracy analysis was carried out on a solution of glucose powder and de-ionised water. The conclusion of the experiment was that the *SNR* should be greater than 15000:1, over a spectral range of 4200cm^{-1} to 4800cm^{-1} (λ = 2083nm to 2381nm). This ratio is obtained from equation 4-5, it is the SNR needed to detect a change in concentration suitable for the accuracy of glucose sensors. Partial Least Squares (PLS) calibration (instrumental) was used to achieve accuracy of 5 mg/dl with an optical path-length of L = 1mm.

Prediction accuracy can also be improved by mathematical optimization (Genetic Algorithm), to achieve an accuracy of 5 mg/dl with a *SNR* of 6500:1. However these figures are based on a test of L = 1mm on a simple glucose solution outside of the body. Inside the body these measurements become more complex and subject to error. A source of error for the experiments is the radiation produced by the human body itself (heat). The spectral range that was focussed on was from 2083 to 2381nm wavelength, outside the near-infrared range.

The journal article details a further set of experiments to determine the effect of increased complexity on the ability to sense glucose. The first test was done with glucose powder dissolved in de-ionised water. The second was done with a blood-like solution of glucose, de-ionised water, bovine haemoglobin and albumin. A third test used actual human blood serum that had been separated by a centrifuge technique.

4.2.4 Experiment Conclusions

Several conclusions were reached from the experiments:

- An increase in sample complexity causes a decrease in measurement reliability, because of interfering factors, measuring selectivity and sensitivity, and modelling space requirements.
- Reliability of results varied with different people and different parts of the body. The most reliable body parts tested were the palms and inner arms.
- The strongest signals came at signal wave-numbers of around 7500 cm^{-1} (a wavelength of 1333 nm).

4.3 Spectrophotometers

Spectrophotometers are devices that measure the intensity of light as a function of the wavelength of that light. The system designed in sections four and five is simply a purpose-built spectrophotometer for the near-infrared range.

A common component of a spectrophotometer device is the monochromator. This is a type of mechanical filter that isolates a particular wavelength of light, and can often be tuned to a specific frequency / wavelength of light, with a high accuracy. Basically these devices use a set of mirrors which turn independently to direct light towards a specific direction. The light is shone through a refractive material to split up the spectrum into various components, and the component of light intended is directed toward a receptor. Devices exist where the light is split into its spectral components both at the transmitter and receiver.

Some devices for laboratory experiments will also use a pulse Fourier-transform technique. Similar to the photo-acoustic spectroscopy explained in Chapter 3, this works by hitting a sample with a pulse of radiation and measuring the resulting light (impulse response in control theory) from the sample. When hit by the pulse of energy, the theory is that the sample will then send out its own energy at the characteristic frequencies of the medium.

4.4 Pulse Oximeters

Commonly pulse/heart rate and SpO_2 are measured using the same device, a pulse oximeter. The term SaO_2 is often used to describe the blood oxygen saturation; SpO_2 means that it has been measured using pulse-oximetry.

Pulse oximeters work on the basis of how much red and infrared light is absorbed when this light is shone though some part of the body. Usually light is shone though fingers or ears, obviously to cut down on the light intensity needed. In some cases, light is even shone through on the forehead and the reflected light is measured. Most of the light will be absorbed by tissue, bone and venous blood, but these values of absorption are relatively constant. Arterial blood however has a pulse to it, and its rate of absorption of light can be measured. The basic system is shown in Figure 4-1:

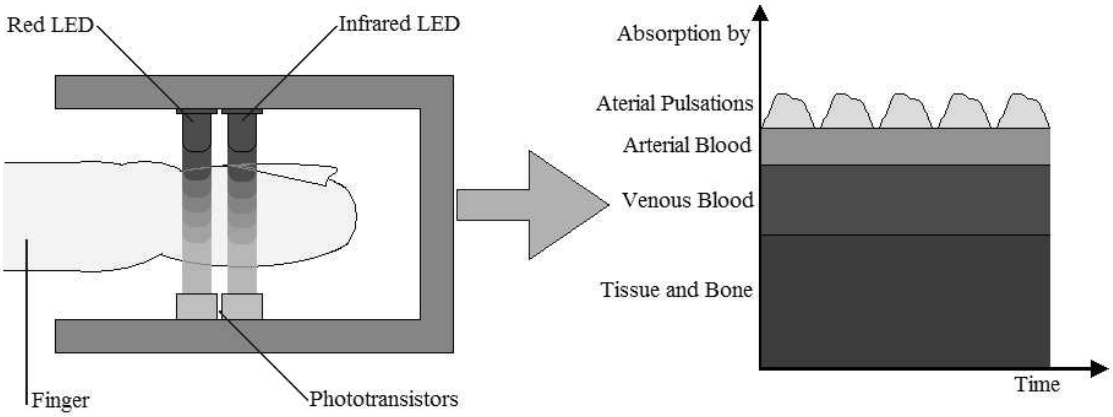


Figure 4-1 Illustration of concept behind pulse oximeter devices

Two LEDs, one red and one infrared shine light through the finger, which is detected by phototransistors on the other side. The amount of light absorbed is determined and from the small pulsations in the signal we can determine pulse rate. The point of having LEDs of different wavelength is to measure the SpO_2. Oxygenated haemoglobin absorbs more infrared light than red light. Deoxygenated haemoglobin absorbs more red light than infrared light.

If the patient is too cold, a natural mechanism for the body is to reduce the blood flow to extremities. This may cause false readings in the device. Integration of a thermal measuring device may be able to moderate false readings.

4.4.1 Other Student's work

A thesis written by University of Queensland student Matthew Roy Burey (Burey, M, 2001) looks in detail at photo-plethysmographic (pulse-oximeter) devices. The focus is on the use of pulse oximeters in monitoring sleep apnea (difficulty breathing, loud snoring) in children. One of the claims made though is that the oxygen saturation of the blood directly corresponds to the volume of intake air. This being the case would mean that there may not need to be a separate sensor or set of sensors to measure breathing; to determine breathing characteristics might only need some simple computer algorithms. The thesis also deals with remote monitoring of patients via the internet; mentioned is the OI^2 (Oximeter Internet Interface) system which connects monitoring devices to a web server via an RS-232 serial interface.

4.4.2 Hospital Visit

To see oxygen sensors and other devices in action, I visited the Toowoomba Base Hospital accompanied with my project supervisor Dr Selvan Pather to talk with some of the staff in the

critical care ward. At the hospital they use a complex monitoring system to monitor various vital signs of the patients. The system uses various modules that feed into a central system which can log the patient's measurements, and also display them in real time for nursing staff and doctors to be able to respond to. Individual modules do all necessary processing in themselves on the signals, to be able to be displayed in monitors or sent to the base unit for recording. These modules are designed to detect a number of different vital signs individually including respiration, ECG (we were shown a 3-lead system) for heart monitoring, blood pressure (both through cannulas and arm pressure pumps), body temperature and of course pulse oximeter readings. As a side note, one thing that was noticed was the mass of leads going to all different parts of the patient's body, and the potential hazards this presented. I believe there could be opportunity for future work in wireless body local area networks to overcome this problem.

The nurse explained the problems with the pulse-oximeters. One of them being the unusable measurements when the patient is moving (she gently shook a patients hand which had one of the devices connected and it made the display of pulse rate and SpO_2 go from being a regular pulse to a random mess). Another is when blood supply to extremities is cut down (elderly people commonly have cold fingers as a result), which would give unrealistically low values of oxygen. A solution they use at the hospital is a second sensor that clips onto the ear rather than the finger. Blood supply to the ear is maintained longer than the fingers when the body gets cold. She also mentioned the ability to take reflective measurements on the forehead.

4.4.3 Application to Glucose Sensor of Pulse Oximeter

Oxygen levels may be easier to detect with infrared light than glucose, indicated by the extensive use in hospitals at present. But the basic method is the same. The wavelength of light used would be different because the molecule we are searching for has different resonance properties.

The next step is to come up with some sort of hardware and software design for the sensor. Details of this design are given in Chapter 5.

4.5 Useable Wavelengths of Light

Infrared light, or near infrared light is used for measurements in the body, because of its absorption properties in flesh, blood and water. In a study of linear polarized near-infrared

light by researchers at the University of Tokyo (Arita, H: Hanaoka, K 1998), it was found that the most effective wavelengths for ray therapy were between 600 and 1600nm, based on the absorption rates of water and blood samples. Figure 4-2 is a reproduction of a figure from the study which shows how light absorption in blood and water samples is affected by wavelength. The term near-infrared pertains to the region of the electromagnetic spectrum with wavelengths from 700 to 1400nm. This overlaps just slightly with the visible spectrum which has wavelengths from 400 to 750nm.

A point for discussion of Figure 4-2 is the rough shape of the curves. The reason for the seemingly random troughs and peaks is the way that light is absorbed in the mediums. Water molecules react in a number of ways to light. For example, the trough at around 3μm in light penetration shown on the water curve is caused by the covalent bonds in the molecule stretching (refer to Figure 4-3). The trough at 6μm is caused by an increase in molecule bending. Some of the others are dependent on rotations of the molecule in different axes. The other smaller troughs are caused by the harmonic overtones of these, such as the one at 1.4μm which is the first overtone of the stretching which occurs at 3μm.

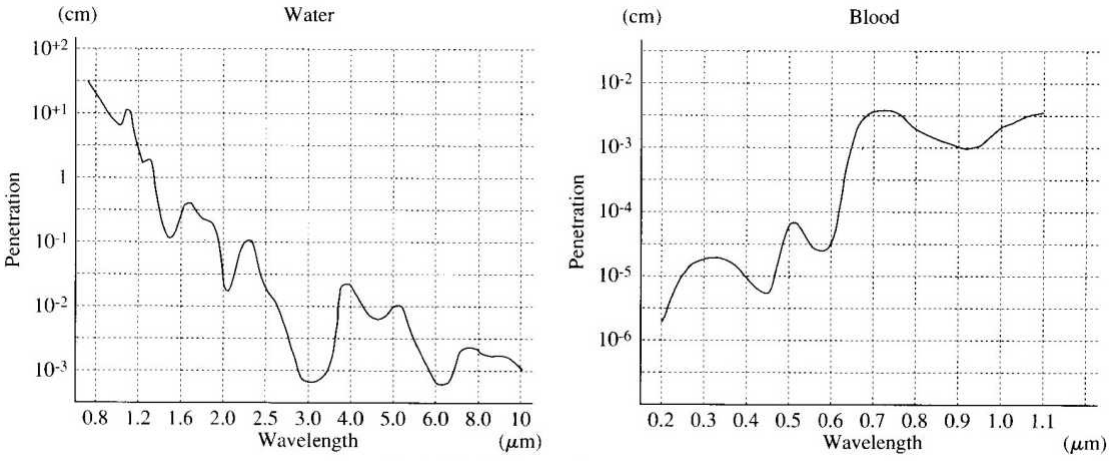


Fig. 5 Light absorption wavelengths

Figure 4-2 Absorption of varying wavelengths of light in water and blood (Arita, H & Hanaoka, K, 1998)

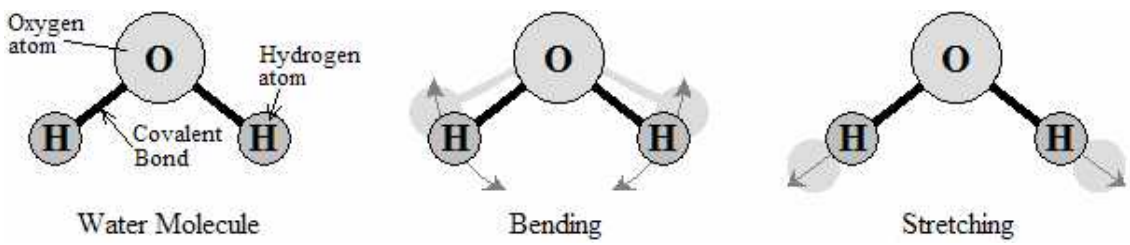


Figure 4-3 Illustration of the absorbance responses of a water molecule to incident light

The near-infrared range has properties that make it suitable for use in the human body. And the studies by researchers at Tianjin University (introduced in section 4.2) suggest the best measurements are taken toward the higher wavelengths in the range.

4.6 Conclusion

A major aim of this project is to conduct testing of glucose measurements. The focus of the project is on the near-infrared spectroscopy method of measuring glucose. An advantage is the versatility of the technique to be used for other purposes. To be able to do this, an infrared sensor system must be developed. This system will need to be very sensitive to voltage signals and be able to be calibrated to different people. A similar device to look at for a starting point is the pulse-oximeter system which is used today in hospitals all over the world. Section 4.4 Pulse Oximeters was taken from work on my initial project choice (*Wireless Measurement and Reporting of Vital Signs During Exercise*). The next chapter will discuss some conceptual designs for measuring glucose in the blood, using near-infrared light.

Chapter 5 : CONCEPTUAL SYSTEM DESIGNS

5.1 Introduction

The conceptual designs in this chapter are aimed at analysing a test sample using infrared light and communicating the results through various interfaces to the diabetic or their carer. Designs assume that the light sensors will work; design and testing of simple sensor circuits is handled in later chapters.

I have considered the design of two different systems with microcontrollers, just briefly, but the testing for the system will actually be done using an analogue to digital converter interfaced directly to personal computer's printer port. If testing of the samples available yields positive results, the algorithms used for analysing samples on the personal computers could be programmed into the microcontrollers, so their design has significance for the future.

5.2 Design Criteria

The best way to start designing the sensor system is to look at its needs and purposes. A sensor system will need:

- To have the accuracy to be able to 'see' the glucose – a processor with ADC capabilities with high resolution. An ADC or analogue to digital converter will take an analogue voltage and through internal comparator circuitry will output a binary number corresponding to the input voltage and a reference. The resolution is how many different levels within the reference range the output can be expressed as. For example, if the reference voltage is 2 volts, and the resolution is 8-bit, then there are 256 different levels available, or an accuracy of 2 V / 256 = 7.8mV.

- To be able to supply enough power to the sensors for them to shine light through tissue.
- Sensors that transmit light at the desired frequencies. The choice of components for the sensors I designed are analysed in a later chapter. Another solution may be to use a monochromator as in spectrophotometers, where the light source produces a wide range of wavelengths, and the unused wavelengths are filtered out with mirrors and diffraction gratings. Due to the cost of existing devices, the system I will use will not contain a commercially available mechanical monochromator. I may use a diffraction grating as a simplified version of the monochromators, if positive results from testing with a simpler system are obtained. I have attempted simulating monochromator operation by using different LEDs to transmit light at different frequencies.
- Ability to interface to a PC (through serial link or wireless), so that results can be analysed by software algorithms.
- To be able to sample at a rate high enough that blood pulse rate can be identified (the pulse may have an effect on the concentration of glucose). I could not find any information on whether pulse rate effects the glucose concentration, but it would be useful to know if it did.
- To possibly have some readout of glucose concentration (as an LED display or otherwise).
- Possibility of programming for a PDA device to be able to give basic analysis.

Designing the sensor can be split into two main areas; hardware and software (the programs needed for controlling the sensors, at a microcomputer level). My recent study of microcomputer systems in ELE2303 Embedded Systems Design is the basis of the design process.

5.3 Sampling Interval

The sampling interval needed for the sensor system may not be particularly small, or small enough to be a critical component in the design. A sampling interval can be roughly determined using the pulse rate of blood in the body. The pulsation of blood in the body would be at a maximum of around 200 beats per minute. This equates to 200/60 = 3.333 beats per second. Sampling theory tells us that the minimum sampling frequency is double the highest frequency of the signal, but a good rule of thumb is to use a sampling frequency 5 to 10 times

the highest frequency of the signal. Hence sampling frequency for the sensors would be 33.333 Hz, or a sampling interval of 30ms. It would not require a very fast microcontroller to achieve this sampling interval.

An important step is to look at the available hardware. A Motorola based system may be a good option, due to familiarity, but there are many other options available. Most of the hardware needed for this design is available from FUTURLEC, an online electronics store, with a base in Australia.

5.4 PICMICRO Controller (MICROCHIP)

One promising controller for the design is the PICMICRO PIC16C765. It is relatively inexpensive (approx. $7 per unit), has pins for a USB 1.1 serial interface, has in-circuit serial programming, and has 8 inputs for an 8-bit analogue to digital converter (the main reason for having a microcontroller). The company that sells these devices also sells development boards for programming aids, which will be essential to developing a system quickly and cheaply. If the design proves to be a success, PCBs (Printed Circuit Boards) could be developed later. A block diagram of the PICMICRO is given Figure 5-1.

This PICMICRO device contains 5 different ports: PORTA, PORTB, PORTC, PORTD, and PORTE. These ports contain multiplexed digital and analogue input and outputs. PORTA contains 5 possible analogue inputs, each with an 8-bit analogue to digital conversion. The remaining three analogue inputs are on PORTE. These analogue inputs are multiplexed so they can also operate as Bi-directional digital I/O. PORTC contains the USB I/O and receive/transmit signals.

5.4.1 Analogue to Digital Converter

One of the first things I needed to look for in a microcontroller is that it has A/D converter capability and what the resolution of this A/D converter is. The resolution tells us how accurate the measurements can be. Consider the graph in Figure 5-2. It illustrates the accuracy of an A/D converter with 4-bit resolution. The curved line represents the analogue input and the filled columns represent the decimal approximation. The sampling space has been tuned to an interval of 0 to 100, so the digital approximation is only accurate to 100/4bit = 100/16 = 6.25.

If an A/D converter does not provide for a high enough signal resolution, data can be multiplexed. The reference voltages for the analogue to digital converter will be an important part of the determination of signal resolution needed. The signal resolution will determine the accuracy of results. A feedback signal controlling the reference voltages may be able to reduce the signal resolution needed. I have assumed that an 8-bit A/DC (2^8 = 256 different voltage levels) will be adequate.

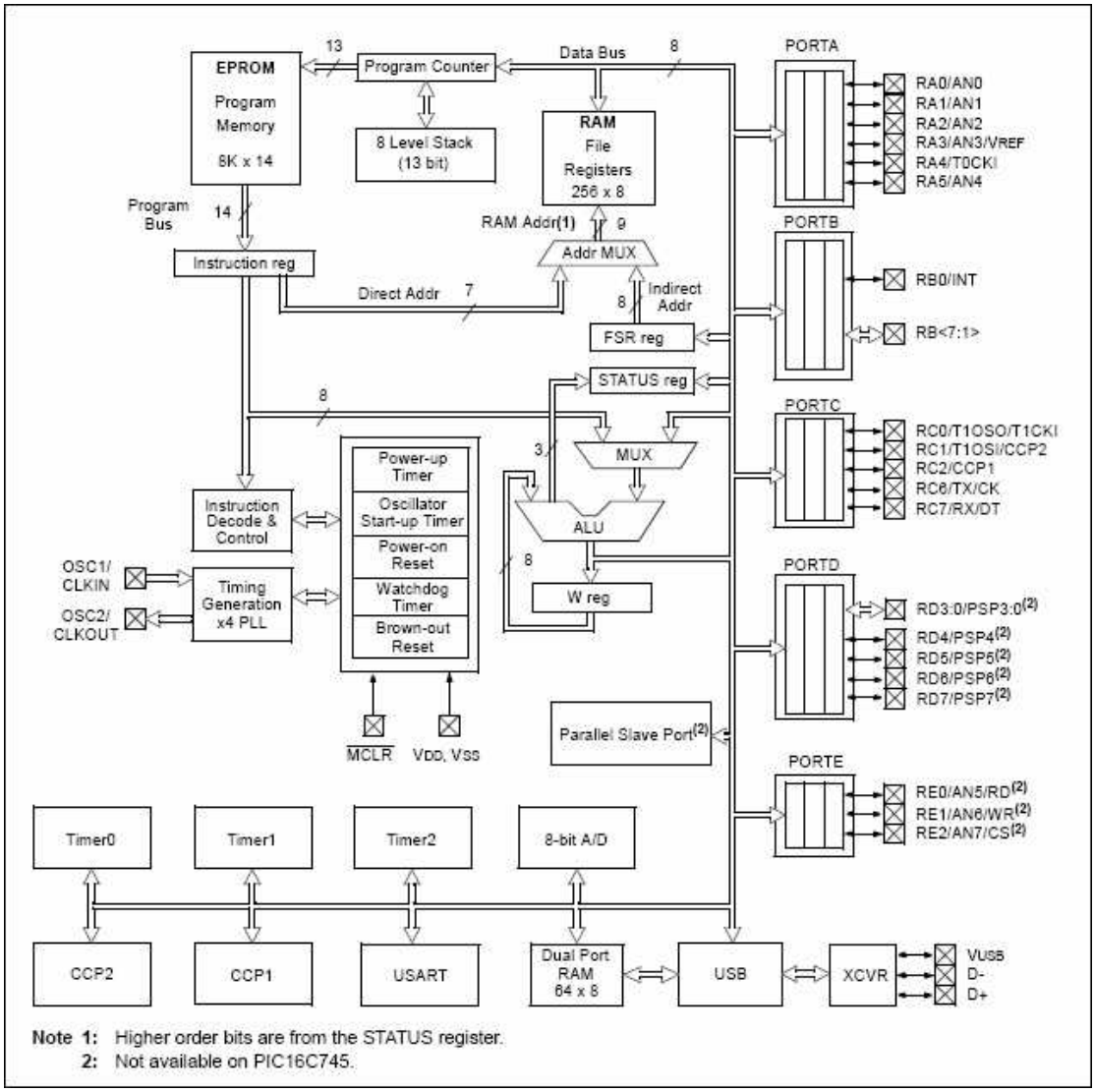


Figure 5-1 PIC16C745 / 765 block diagram

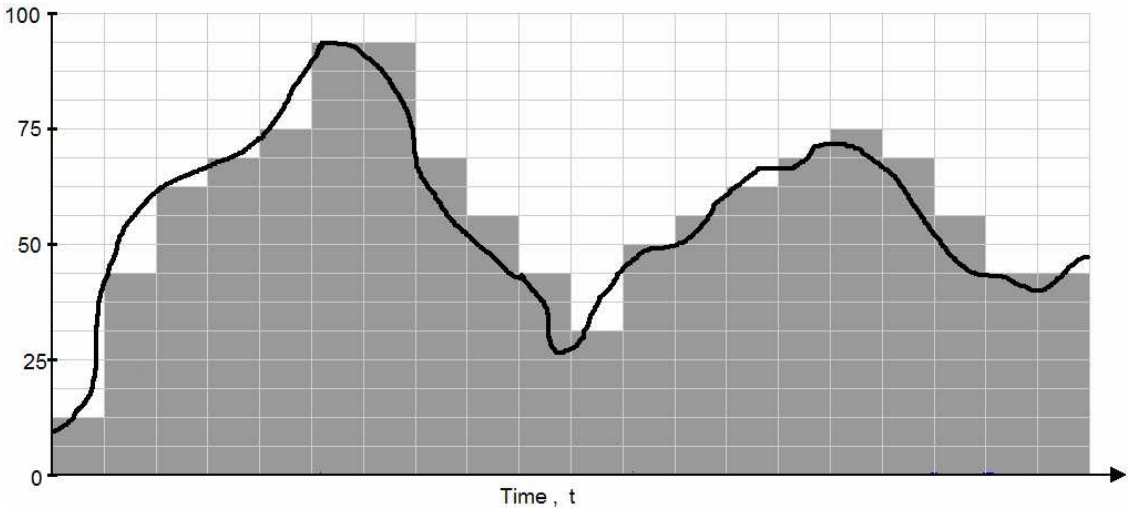


Figure 5-2 Explanation of ADC resolution. Data is not important.

When using the ADC, we need to allow time for the capacitor to arrive at the correct voltage. This time is given by the equation:

$$\begin{aligned} T_{acq} &= T_{AST} + T_C + K_T \\ &= 5\mu s + \left(-C_{HOLD} \ln\left(\tfrac{1}{512}\right)(R_{IC} + R_{SS} + R_S)\right) \\ &\quad + \left(\left(Temp - 25^\circ C\right) \times 0.05\mu s / C\right) \end{aligned}$$ **.....EQ. 5-1**

Where T_{AST} = Amplifier Settling Time = 5µs

T_C = C_{HOLD} Settling Time

K_T = Temperature Coefficient

C_{HOLD} = Sample/Hold Capacitance

R_{IC} = Interconnect Resistance

R_{SS} = Sampling Switch Resistance

R_S = Resistance on input voltage

The initialisation of the peripheral registers on the PICMICRO for ADC inputs on PORTA requires writing to ADCON1 or address $0x9F.

5.4.2 IR LEDs Interface

The near-Infrared LEDs will be connected to PORTB. This port is suitable only for bi-directional data Input/Output. The LEDs will connect to the port as shown in Figure 5-3. There are in the diagram four LEDs and four receiving lines. The reason for having multiple lines for

the sensor is to test the effect of different wavelengths of light on the signal received.

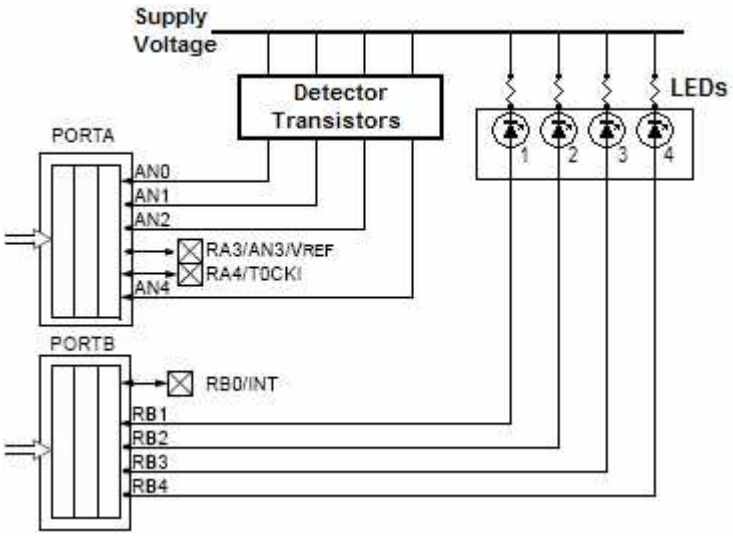


Figure 5-3 Connection of LEDs with PICMICRO

The output voltages of the I/O lines are 0 to 0.6V for a low, and for a high, greater than V_{DD} – 0.7V. Maximum output sourced and sunk by any I/O pin is 25mA, while PORTA, PORTB and PORTE have a maximum combined sink and source current of 200mA. PORTC and PORTD have a maximum combined sink and source current of 200mA. These currents are absolute maximum ratings.

The detector transistors could also be photodiodes. In the case of photodiodes, the open circuit voltage is directly proportional to the amount of light energy incident with the photodiode surface, though it is over a fairly small range. Setting the reference voltages at the limits of this range will give the maximum accuracy.

5.4.3 LED / LCD Readout

An option for the device is to have LED or LCD readout of glucose percentage. The percentage will be expressed as relative to the healthy level of glucose in the blood. While developing the simple test circuit in Chapter 6, I used an analogue to digital converter chip to output a digital bit pattern, with the intention of being able to send this to a personal computer. To see immediately what the output was, I connected a red LED to each of the data lines of the ADC. This gave a bit pattern as a combination of on or off signals from the LEDs.

For a device which could be used by diabetics though, it would not be helpful if the output was in binary; most people, myself included, can not read and recognise binary numbers without having to sit down and think for a while.

Available from FARNELL are a range of small LCD displays that could be driven by the microcontroller. Prices start at about $30 for a 16-digit screen; this would be adequate for a glucose meter, as all it needs to display is a percentage. The current requirements for such a device can be supplied by the microcontroller – one particular LCD display, the TRIMODS1531, requires a total forward current of 88mA: the PICMICRO can source and sink up to 200mA on its ports. The LCD has five power supply lines (two for the LED backlight, one for the chip, one for the LCD and another for ground), three “handshake” lines (i.e. R/W, RS and E), and eight data input lines.

5.4.4 In Circuit Serial Programming (ICSP)

The PICMICRO provides in-circuit serial programming. This will be useful for the project because I will be able build the system while still modifying the program, saving time. The programming requires two lines for clock and data and three other lines for power, ground and programming voltage. The connections needed for this are given in Figure 5-4. This program will be written to an EPROM. The OTP (One-Time-Programmable) package only lets the programmer load the program once, but a UV (Ultra-Violet) erasable CERDIP (Ceramic Dual-In-line-Package) allows reprogramming. The UV erasable CERDIP package is more expensive.

But, in development, I will likely be reprogramming the system often to optimize it and to develop suitable control systems. For this reason an off-chip memory device may be needed to store changing program data (for the program development stage).

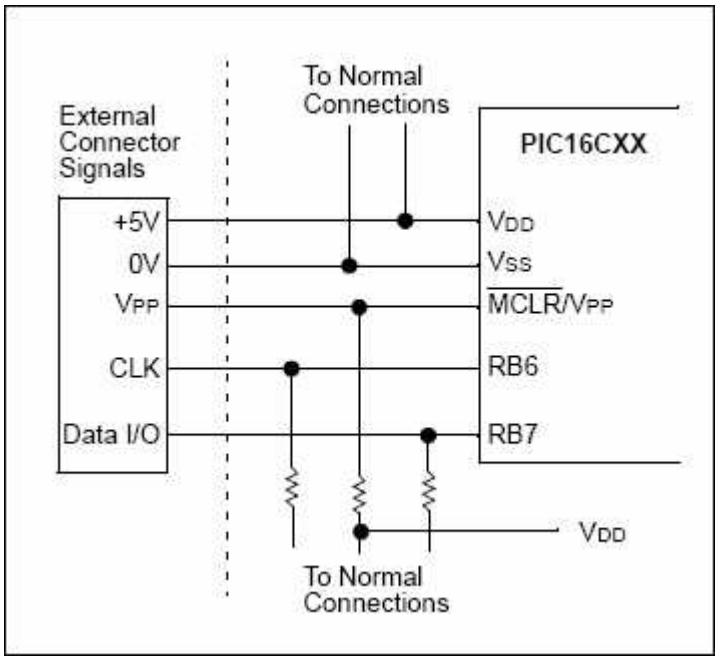


Figure 5-4 Connections needed for ICSP

The ICSP uses lines RB6 and RB7 of PORTB. There may be yet some clash between using these ports and the first four for LED lines.

5.4.5 Communication with PC

To analyse the data obtained from the sensors, I will need communication to a PC. The available connections are a USB serial link, a USART serial link, and an 8-bit parallel link on PORTD.

The USB link is best for control signals and interrupts. To overcome problems with the OTP program memory storage, all different possible cases could be programmed into the EPROM and which ones are used could be just determined using the control signals.

5.4.6 Programming Module

The term programming module in this context describes the programming software for direct use by the microcontroller, not the computer controlled systems used for analysing data on the PC (Personal Computer). The program ‘MPASM’ is used to write software for the PICMICRO.

5.4.7 Memory

The PICMICRO has 8K of EPROM, each location being 14 bits long. It also has 256 8-bit memory locations in RAM for data.

5.4.8 Suitability for Project

A PICMICRO controller would be suitable for this project, though I would need to learn a new programming language. Since it is not the aim of the project to learn how to use a particular microcontroller device, rather to create or assess the viability of a diabetes sensor, using a more familiar device; that is, a Motorola, might be a better option.

5.5 Motorola 68HC908

A Motorola based system may be a good option, due to familiarity; an 8-bit Motorola microcontroller was the main focus of unit ELE2303 Embedded Systems Design which I studied in semester 1 2005. Futurlec has a number of different 68HC908s available, several of them with inbuilt A/D converters and suitable peripheral ports, to minimise additional circuitry. They are also fairly inexpensive (<$10). A block diagram of the Motorola MC68HC908GR8, a package with 8kB of flash program memory and built-in A/D converter is given in Figure 5-5.

Like the PICMICRO, the Motorola device has five separate ports (32 pin QTP package). But the project would use the 28 pin package that has two less analogue inputs on PORTB and no PORTC.

5.5.1 Analogue to Digital Converter

The analogue to digital converter is 8-bit with 4 channels, and receives its inputs through PORTB. Analogue signals will come via a specialised resistor called a photocell. These photocells have a resistance that varies inversely with light intensity; as light intensity increases, resistance decreases. According to available information; the accuracy of received signal is dependent only on the resolution of the ADC. The voltage range can be tuned using a voltage divider circuit. Photocells need to be tuned individually though, as their response to light intensity can vary. An important consideration for these devices may be a shield to block out ambient light, if it is found to affect measurements. The basic setup for an analogue input of a photocell is shown in Figure 5-6.

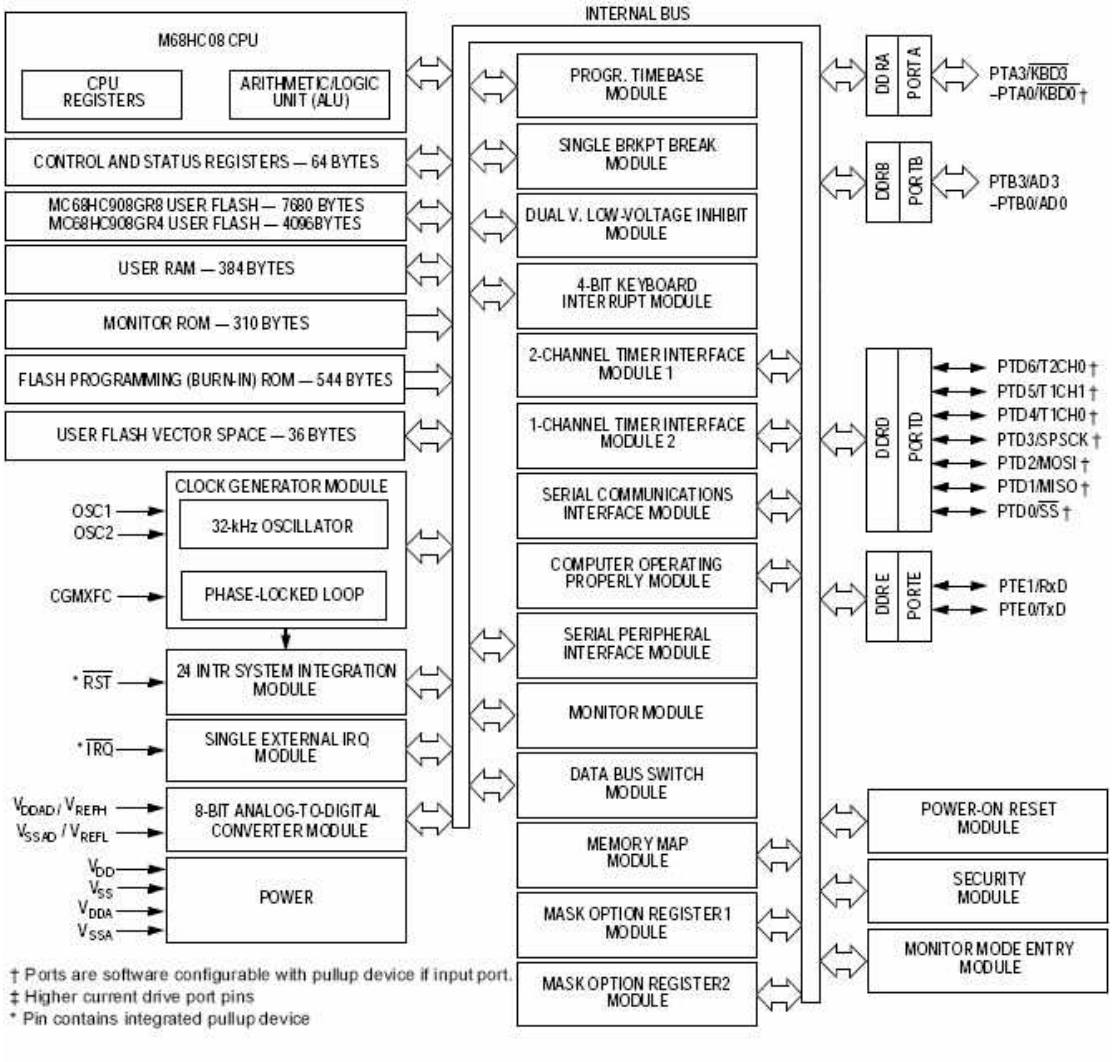


Figure 5-5 MC68HC908 block diagram

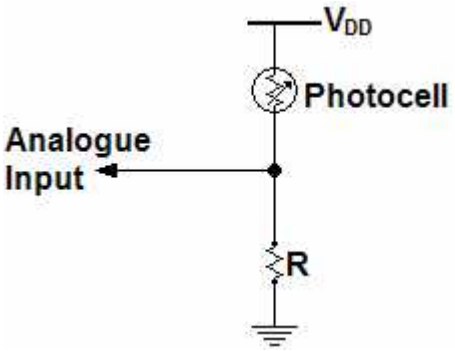


Figure 5-6 A photocell basic circuit

5.5.2 IR LED Interface

The Infrared LEDs will be connected to the peripheral PORTD. The sensor would be constructed with four different IR LEDs to see the effect of different wavelengths of light. Because of this, there will also be four photocells to respond to the IR light. Connection of the

LEDs and photocells are shown in Figure 5-7. There is an assumption that an ordinary infrared LED will be powerful enough to penetrate though any tissue. Results of the testing phase may lead to using different peripheral components (LEDs and Photocells) that are more suitable.

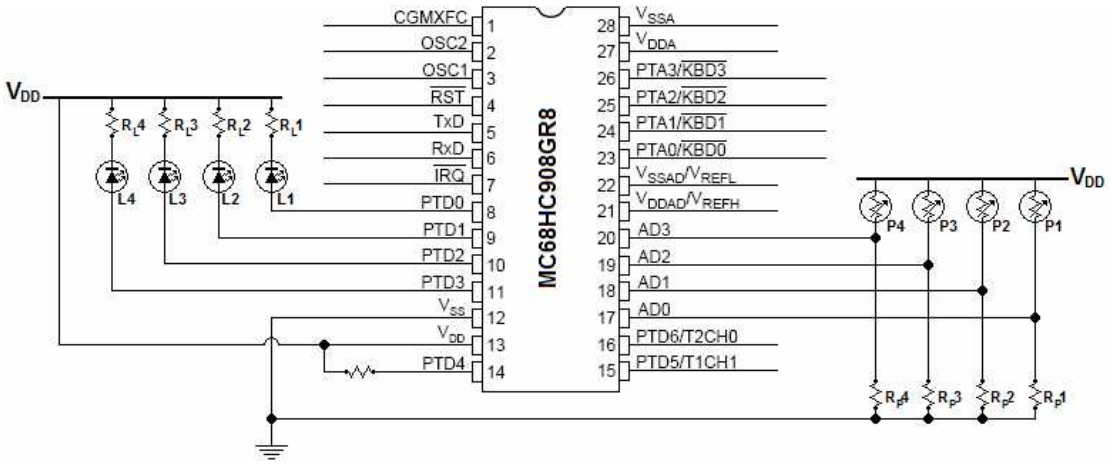


Figure 5-7 Connection of LEDs and photocells to the microcontroller

5.5.3 Interface between Microcontroller and Personal Computer

The link between the Microcontroller unit and a personal computer can be accomplished through the Transmit Data (TxD) and Receive Data (RxD) lines, which together form the I/O of the Serial Communications Interface (SCI). Of course an important consideration is what happens at the other end (how the personal computer is going to handle it). This will be addressed in the next section. Basically though, it can be assumed that connection to a parallel port of a computer will provide the sensor with communication lines and power.

The communications link will provide three main functions:

- Collection of data from sensors to the PC
- Programming the controller
- Providing interrupts

The collection of data will be done through the SCI on TxD and RxD. Programming the controller in circuit requires bit 0 of PORTA (to Monitor ROM function).

5.5.4 Programming the Controller

Programs can be stored in the flash memory on the chip. The ‘GR8’ controller has 8kB on board flash memory that can be programmed in circuit.

To program the FLASH memory, the following sequence must happen:

1. Set the PGM bit. This is bit 0 of the FLASH control register, which is mapped to location $FE08
2. Read from FLASH block protect register (FLBPR, $FF7E)
3. Write any data to the FLASH address within the row address desired
4. Wait for at least 10µs (t_{nvs})
5. Set the high voltage enable (HVEN) bit of FLASH control register (bit 3)
6. Wait for at least 5µs (t_{pgs})
7. Write data to the FLASH address to be programmed
8. Wait for at least 30µs (t_{prog})
9. Repeat steps 7 and 8 until all bytes in the row are programmed
10. Clear PGM bit.
11. Wait for at least 5µs (t_{nvh})
12. Clear the HVEN bit
13. Wait for at least 1µs (t_{rcv})

This complete sequence is used to program one row of data, and must be restarted for each row. Each row is 32 memory locations long. Appendix B of this project contains a program written in assembly language based on the sequence given above for programming the microcontroller (FLPROG). It also contains code developed for a similar program to erase flash memory.

5.5.5 Cost of Components

To build and develop the Motorola-based glucose sensor, I would need the following components: microcontroller, photocells, IR LEDs, parallel data link, an oscillator chip, a breadboard, and various resistors and capacitors. If the components were purchased through the online Australian electronics company, FUTURLEC, all components could be purchased for under $30, based on the minimum order prices. In developing the circuit, there would likely be failure of some components. The total order cost, allowing for some failures of components is $56.26.

5.6 Direct Connection to PS2 Parallel Printer Port

At a later stage, a system based on a microcontroller would be essential to make the diabetes sensor compact. But for testing of glucose samples, there is no need to make the electronics any more complicated. Basically, the previous two designs, though not taken to the point of being workable, had the same idea in mind: use an 8-bit ADC to measure the amount of light absorbed by a sample, and send it via a serial link to a PC for mathematical analysis. A simpler way of doing this is to connect an 8-bit ADC integrated circuit directly to the PS2 parallel printer port of a personal computer.

5.6.1 Parallel Printer Port

Most parallel printer ports in use today comply with the IEEE 1284 standard. Ports made to this standard have up to 36 pins available (1284 B), including 8 data lines which can be made bi-directional, if run in the right mode. There are five different modes that these ports can operate in, and when engaging a printer, the computer will decide which one is needed, based on available drivers. Pin assignments are defined in software. A list of the pin assignments (for bi-directional mode) is given in Table 5-1.

Table 5-1 PS/2 parallel port pin assignments

Pin	Function		Pin	Function
1	Host clock		19	----------
2	Data 1		20	----------
3	Data 2		21	----------
4	Data 3		22	----------
5	Data 4		23	----------
6	Data 5		24	----------
7	Data 6		25	----------
8	Data 7		26	----------
9	Data 8		27	----------
10	Pointer clock		28	----------
11	Pointer busy		29	----------
12	Acknowledge data request		30	----------
13	X-flag		31	Initialise
14	Host Busy		32	Data available
15	----------		33	----------
16	----------		34	----------
17	----------		35	----------
18	----------		36	1284 Active

5.6.2 Analogue to Digital Converter

The ADC0804LCN is an 8-bit analogue to digital converter, available from FARNELL. Output of the device is a eight parallel data lines.

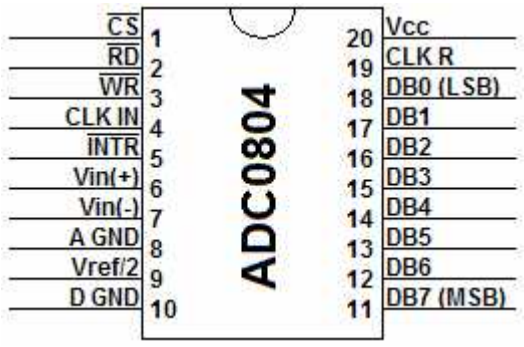


Figure 5-8 ADC0804 8-bit analogue to digital converter

5.6.3 Parallel Port Connection to ADC

Figure 5-9 shows a way of connecting the ADC0804 to the parallel port of a computer. The eight data lines are connected through resistors (R_D) to the data lines of the parallel port. The data lines have a minimum source current of 4.5mA. To limit the current to this, the resistance (R_D) chosen would be the output voltage, 4.5V divided by the source current 4.5mA, which works out to be 1kΩ.

Power is received through the 1284 active line of the port. This line is used to power the ADC circuit, the photocell and the IR LED.

When the CS and RD lines are all tied to the Init line, a logic 0 on the Init line will enable a read of the analogue inputs and a start for the analogue to digital conversion. Tying the INTR line to the WR line will mean that the system will operate in free-running-mode; that is, as soon as the ADC converts a voltage it will write it to the data bus, with no further input from the host.

The ADC has its own timing circuit, provided by R_C and the capacitor. The operating frequency of the ADC can then be modified with the choice of R_C and C:

$$Frequency,\ f = \frac{1}{1.1\,R_C C} \quad \text{.....EQ. 5-2}$$

The operating frequency of the parallel port running in byte mode is typically between 50 kHz and 150 kHz. To have the ADC running at 10 times this speed would ensure no problems with timing. If R_C is chosen to be 10kΩ, then C will be:

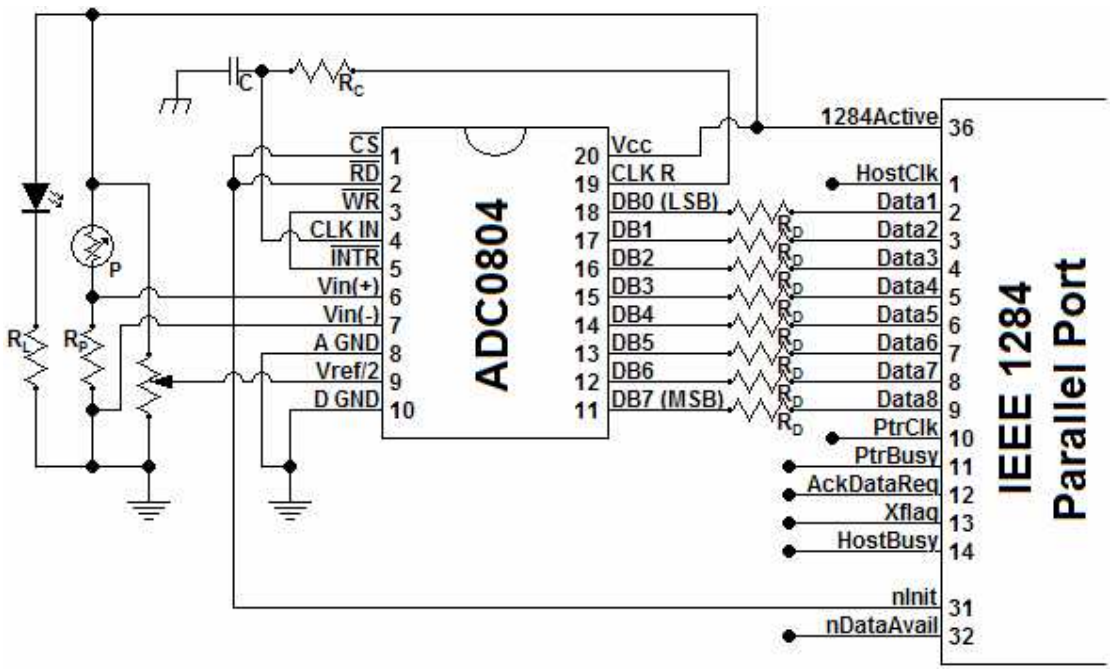


Figure 5-9 Parallel port connection to the ADC0804

Frequency, $f = 1500\ kHz$

$$Capacitance,\ C = \frac{1}{1.1\,R_C f} \quad \text{.....EQ. 5-3}$$

$$C = \frac{1}{1.1\times\left(10\times10^{3}\right)\times\left(1500\times10^{3}\right)}$$
$$= 60\,pF$$

A host clock signal is then not needed for the device. Instead, the nInit line is used to tell the ADC that it is ready to accept information. Other outputs of the parallel port are not needed either. The details of this will be considered in the software design.

5.6.4 Software Design

A program to drive the ADC will operate using this sequence:

1. Set the nInit line (pin 31) high.
2. Activate the 1284 Active line (pin 36).
3. Bring the nInit line low.
4. Read the word made up of data lines 1 to 8 (pins 2-9), and save in specific location.
5. Bring the nInit line High again.

Handshake signals would normally be needed so the ADC has time to complete its transfer of data, but the ADC will operate at a much higher frequency than the parallel port.

For personal computers, the addresses for printer ports can be found at $0378 to $037F. Programming the printer for reading the lines as inputs is very simple in QBASIC. All that needs to be done is to use the commands:

>>out [address of control lines], [number representing required bit pattern]
>>portnum% = inp([address of data port])

The numbers obtained can then be read and analysed. In terms of the hardware, the potentiometer connected to the Vref/2 pin can be used to tune the device to maximise clarity of data.

If the 8-bit resolution was found to be inadequate for measurements (which may be the case when more complex test specimens are used; refer to section 5), there are higher resolution ADCs to use. Since there are only 8 data lines available in a printer port, the maximum resolution that can be obtained is 8-bit, using a parallel connection. To get a more accurate reading, connections need to be serial. The downside is an increase in the complexity of programming, and a reduction in processing speed (though for this purpose the speed is not really important).

5.6.5 Evaluation of Design – Before Implementation

Now this particular design is limited, since it will only test for light intensity over a relatively wide bandwidth. What is needed is a more specialised sensor system, or possibly more sensors incorporated into this design to get a conclusive reading.

One way to solve this problem could be to do a thorough search for better light – detecting devices. Another way is to use the results from this light test as just one measure of the

physical properties of the test subject. To validate results a test for other properties, such as electrical conductance/capacitance, an orefactory test, etc.

The designed system will be important however in determining the capabilities of this type of design, before expensive complex components are included.

5.7 Conclusion

The basics of a sensor-circuit design have been covered in this chapter. Three different sensor-circuit designs have been developed, one based on a PICMICRO microcontroller, another based on an equivalent Motorola microcontroller, and another which just uses a personal computer for its control. The designs would require more detail if they were to be built. To allow testing though, I designed a simplified circuit that measures light intensity through a test substance and converts it to a voltage that can be analysed. The development of this design and justifications of light responsive components used is covered in the next chapter.

Chapter 6 : BASIC SENSOR CIRCUIT DESIGN

6.1 Introduction

An important part of the project will be determining what type of sensors to use and their accuracy. I have focussed mostly on light as a means of measuring physical properties. There are a number of ways to measure light, and this section will explain how they work, so that useful analytical tools can be developed.

6.2 Photo-resistors

In the system that was designed in section 5.3, the sensor used was a photo-resistor. These devices are particularly useful for light detection over the visible range, and infrared ranges, but at much lower frequencies background heat energy will affect measurements. Infrared spectroscopy commonly uses high performance photo-resistors. Cadmium-based photo-resistors are best for the visible and near-infrared range. The resistance of a photo-resistor is non-linear, but can be modelled approximately with EQ. 6-1:

$$Resistance,\ R = A \times E_v^{-\alpha} \quad \text{.....EQ. 6-1}$$

Where A and α are constants, based on the material properties of the photo-resistor, and E_v is the incident light energy, expressed in electron volts. One electron volt or 1eV is equal to 0.1602aJ (0.1602×10^{-18}J). This energy is related to the wavelength of light through the following relationships:

$$Energy\ (in\ Joules),\ E = \frac{c \times h}{\lambda} \quad \text{.....EQ. 6-2}$$

Where c = speed of light = 300×10^{6} m.s^{-1} (approximately),

h = Planck's constant = 6.62×10^{-34} J.s

and λ = wavelength of light

$$Energy\ (in\ eV),\ E_v = \frac{c \times h}{\lambda \times 0.1602 \times 10^{-18}} \quad \text{.....EQ. 6-3}$$

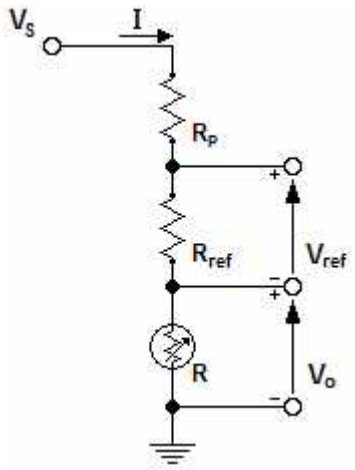
$$Energy\ (in\ eV),\ E_v = \frac{300 \times 10^{6} \times 6.62 \times 10^{-34}}{\lambda \times 0.1602 \times 10^{-18}} = \frac{1.24 \times 10^{-6}}{\lambda}$$

So the resistance will vary with wavelength of light based on equation 6-4:

$$Resistance,\ R = A\left(\frac{1.24 \times 10^{-6}}{\lambda}\right)^{-\alpha} \quad \text{.....EQ. 6-4}$$

To complicate matters though, the resistance also varies by orders of magnitude with light intensity. It is perhaps possible to design calibration techniques to find these relationships

Importantly though, it is the resistance that needs to be measured, not the voltage output. It may sound trivial, but measuring voltage can lead to errors. Fortunately there are methods to measure resistance. The following circuit (Figure 6-1) is one such method employed in resistance measurement. This method, called the two-reading-method is used to calculate resistance in the following manner:



$$V_{ref} = I.R_{ref}$$
$$and \quad V_0 = I.R$$
$$Then \quad I = \frac{V_{ref}}{R_{ref}} = \frac{V_0}{R}$$
$$\therefore \quad R = \frac{V_0.R_{ref}}{V_{ref}}$$

Figure 6-1 Resistance measurement circuit

In this circuit, the reference resistance (R_{ref}) would be made to be equal to the maximum expected resistance of the photocell.

If V_{ref} is connected to the reference voltage of an ADC, then the resistance can be found in software.

Another circuit, commonly used for non-linear resistance measurements is a voltage divider circuit. Figure 6-2 shows a voltage divider. In this circuit, the voltage output is determined by the ratio given in equation 6-5. The photocell resistance will change according to the incident light, affecting the ratio, and hence changing the voltage output.

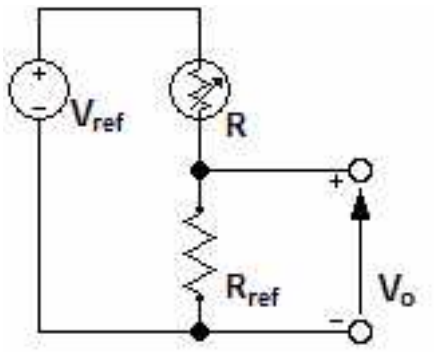


Figure 6-2 Voltage divider circuit

$$V_0 = \frac{V_{ref}}{\left(R_{ref} + R\right)}.R_{ref}$$
$$\therefore \quad R = \frac{V_{ref} - V_0}{V_0}.R_{ref} \qquad \text{.....EQ. 6-5}$$

6.3 Phototransistors

Phototransistors are another common component that is responsive to incident light. But these are not as accurate for measurement as photo-resistors. Phototransistors are much more suited to high speed switches based on optical signals, such as remote control systems or optical fibre transmission of digital data. Gains for these components are often around 100.

A problem with photocells is their availability in the near-infrared range. Many exist that have their peak at around 550nm (within visible light range), the problem being that the wavelength of light to measure is between 850 to 950nm. There are actually some electronics that will build custom photocells, designed for a specific wavelength of light.

6.4 Photodiodes

Another option is to use photo diodes. These are a bit more complex to design for, but are generally more accurate and behave in a more linear manner than a photocell. Photodiodes are already used in the glucose measurement devices that involve pin-pricks. In these common home tests, blood is put on a test strip, which reacts specifically to blood sugar and changes the reflective properties of the strip, which can be measured by using photodiodes.

Briefly, a photodiode is simply a diode that can be used to control current flow in a circuit. All semiconductor p-n junctions, of which diodes consist, are affected by light. When photons hit the semiconductor, they create electron holes and pairs. In most diodes however, the semiconductor is shielded from light to remove this effect. Photodiodes have windows to make use of the light dependant characteristic.

The current through a photodiode when energised by light radiation is dependent on the sensitivity of the diode (S_λ), and the incident light power (P):

$$Current,\ i_P = S_\lambda . P \quad \text{.....EQ. 6-6}$$

The particular diode intend for use in the sensor is a Siemens SFH 203P. Some of the important parameters for this component are:

Maximum reverse voltage, V_R = 5 Volts
Sensitivity, S = 9.5 (≥ 5) nA / lx

Wavelength of maximum sensitivity, $S_{\lambda max}$ = 850 nm

Spectral range of sensitivity, S = 10% of S_{max} is λ_{range} = 400 – 1100 nm

Radiant sensitive area, A = 1mm^2 (square)

Half angle, $\varphi = \pm 75^o$

Dark current, I_R = 1 ($\leq$ 10)

Spectral sensitivity, S_λ = 0.62 A/W (at $S_{\lambda max}$)

Quantum yield, η = 0.89 Electrons / Photon

Open circuit voltage (at E_v = 1000 lx), V_O = 350 ($\geq$ 300)

Short-circuit current (at E_v = 1000 lx), I_{SC} = 9.3 μA

Rise and fall time of the photocurrent (at R_L = 50 Ω; V_R = 20 V; λ = 850 nm; I_p = 800 μA),

t_r, t_f = 5 ns

Forward voltage (at I_F = 80 mA, E = 0), V_F = 1.3 V

Capacitance (at V_R = 0 V, f = 1 MHz, E = 0), C_0 = 11 pF

Temperature coefficient of V_O, TC_V = -2.6 mV/K

Temperature coefficient of I_{SC}, TC_I = 0.18 %/K

Noise equivalent power (at V_R = 20V, λ = 850 nm), $NEP = 2.9\times10^{-14}$ $W/\sqrt{H}$

Detection limit (at V_R = 20V, λ = 850 nm), $D = 3.5\times10^{12}$ $cm\sqrt{H}/W$

So we can generate a photo-current in the photodiode. But of course this cannot be measured by a personal computer's parallel port as intended; we need to produce a voltage that varies with incident light intensity. It can be produced by using a simple op-amp as a trans-impedance device, as shown in Figure 6-3. The particular operational amplifier used in the circuit is a video-amp. A handy property of this op-amp is that it runs on a +5V to 0V ground voltage supply.

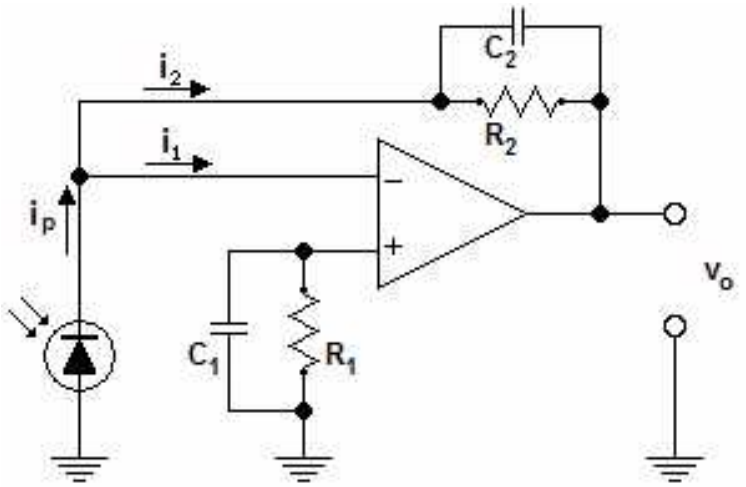


Figure 6-3 Trans-impedance amplifier applied to a photodiode

The circuit can be analysed as follows:

Assume the impedance of the op-amp is high enough such that current going through the inputs is negligible. Then the current i_1 is approximately 0A, and $i_2 = i_P$. Then the voltage across R_2 is:

$$V_{R2} = i_P . R_2 \quad \text{.....EQ. 6-7}$$

The capacitor in parallel with the resistor R_2 is there to eliminate high-frequency noise, and a 10µF is chosen as a rule of thumb. Basically, using a 10µF will produce an output voltage relative to the frequency, as shown in figure 6.4. This will protect the op-amp from significant harmonic and inter-modulation distortion and gain peaking. Capacitor C_1 could be made to be the same value. It is responsible for reducing noise bandwidth.

This circuit has a simple output: $v_o = i_p.R_2$. The range for voltage v_o can then be chosen using the resistor R_2. If a potentiometer is used for R_2, then the circuit can be tuned to allow for unknown currents, i_p. Choosing R_1 to be equal to R_2 will reduce the effect of op-amp input currents to those of its offset currents. The circuit with the trans-impedance amplifier included is shown in figure 6.4.

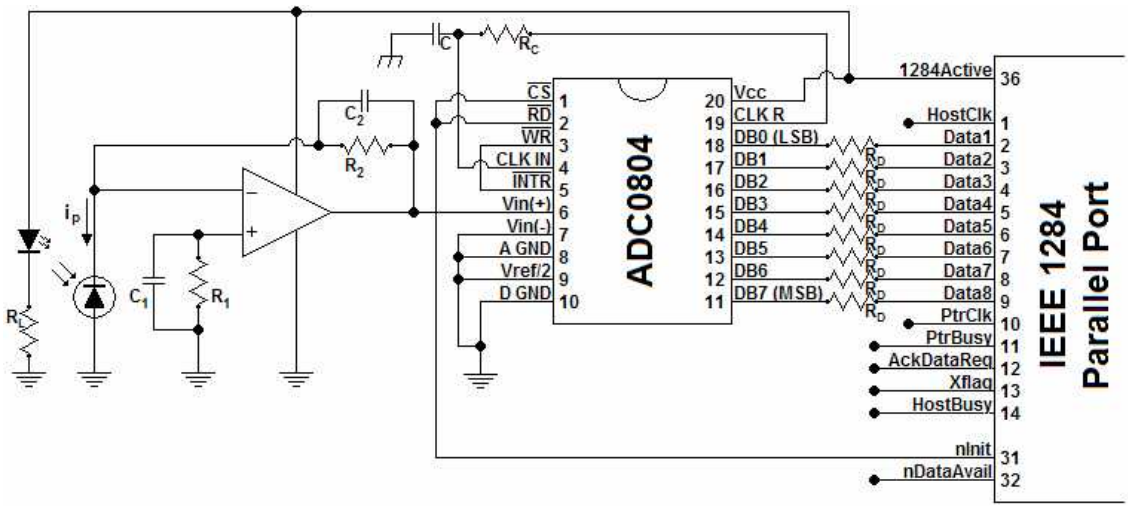


Figure 6-4 Entire Circuit with trans-impedance amplifier

Table 6-1 shows the maximum photocurrent that can be expected when using four different IR LEDs with the Siemens SFH 203 P photodiode. The components listed in the table are available from FARNELL. When the circuit is constructed, it will be designed so that all four of the LEDs can be tested.

Siemens SFH 203 P properties:

Noise Equivalent Power	= 2.90E-14 $W/\sqrt{Hz}$
Sensitivity	= 0.62 A/W
Alpha	= 0.89 electrons/photon
Incident Area	= 1.00E-06 m^2
Peak Sensitivity Wavelength	= 880nm
Maximum Reverse Voltage	= 5.00 V
Dark Current	= 2.80E-10 A

Table 6-1 Theoretical results of four photodiode and LED combinations

LED	$\Delta\theta^o$	*Sr*	I_e (W/sr)	*P* (W)	S_{rel}	i_P (A)	λ (m)
OPE5685	22	0.458	5.00E-02	2.29E-02	9.30E-01	1.32E-02	8.50E-07
TSUS5400	22	0.458	7.00E-03	3.20E-03	9.40E-01	1.87E-03	9.50E-07
OPE5594A	10	0.095	8.00E-02	7.64E-03	9.60E-01	4.55E-03	9.40E-07
TSHA440	20	0.379	1.60E-02	6.06E-03	9.80E-01	3.68E-03	8.75E-07

Δθ° = Sensitivity Half Angle (degrees)

sr = A unit based on the half angle (steradians)

$$1\,sr = 2.\pi.(1-\cos\Delta\theta) \quad \text{.....EQ. 6-8}$$

I_e = Incident light energy (watts / steradian)

P = Incident light power (watts)

S_{rel} is a value determined from a plot of the sensitivity of the photodiode as it varies with wavelength.

i_p = Photocurrent generated in photodiode (amperes). This figure is based on no losses through the air or testing material. All measured values can then be expressed as a percentage of this value.

λ = Wavelength of peak intensity for that particular diode (metres)

From the table, we see that the photocurrent maximums generated by the photodiode range from 1.87mA to 13.2mA. The maximum voltage input to the analogue to digital converter will be equal to its supply voltage, which will be 5 volts. So the required value for resistances R_2 and R_1 will be:

$$R_1 = R_2 = \frac{v_{0(\max)}}{i_{P(\max)}} \quad \text{.....EQ. 6-9}$$

$$R_1 = R_2 = \frac{5}{13.2 \times 10^{-3}}$$
$$= 378.8\Omega$$

The forward current for the LEDs is typically 100mA, so the resistance, R_L needed is

$$R_L = \frac{v_{CC}}{i_F} \quad \text{.....EQ. 6-10}$$

$$R_L = \frac{5}{100 \times 10^{-3}}$$
$$= 50\Omega$$

6.5 Relative Spectral Power Graphs

Data sheets for each LED contain a graph of the relative radiant power versus the wavelength of light. An example for the TSUS5400 LED is given in Figure 6-5. These may be useful in determining the effect of wavelength on voltage output of a sensor. A crude initial method of investigating this relationship is to read the values contained in the graphs. The full table of values read for each LED are given in Appendix C. When these values are entered into an Excel spreadsheet, the graphs can be superimposed on one another. But for the data to be more useable, the values are moderated against the power emitted from each diode. The moderated power curves are shown in Figure 6-6.

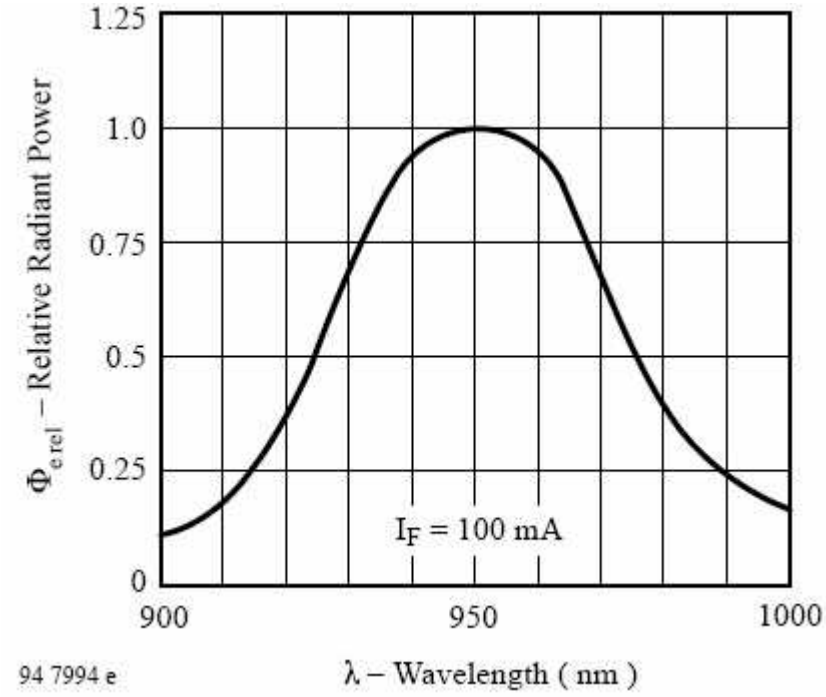


Figure 6-5 Relative radiant power vs. wavelength, TSUS5400

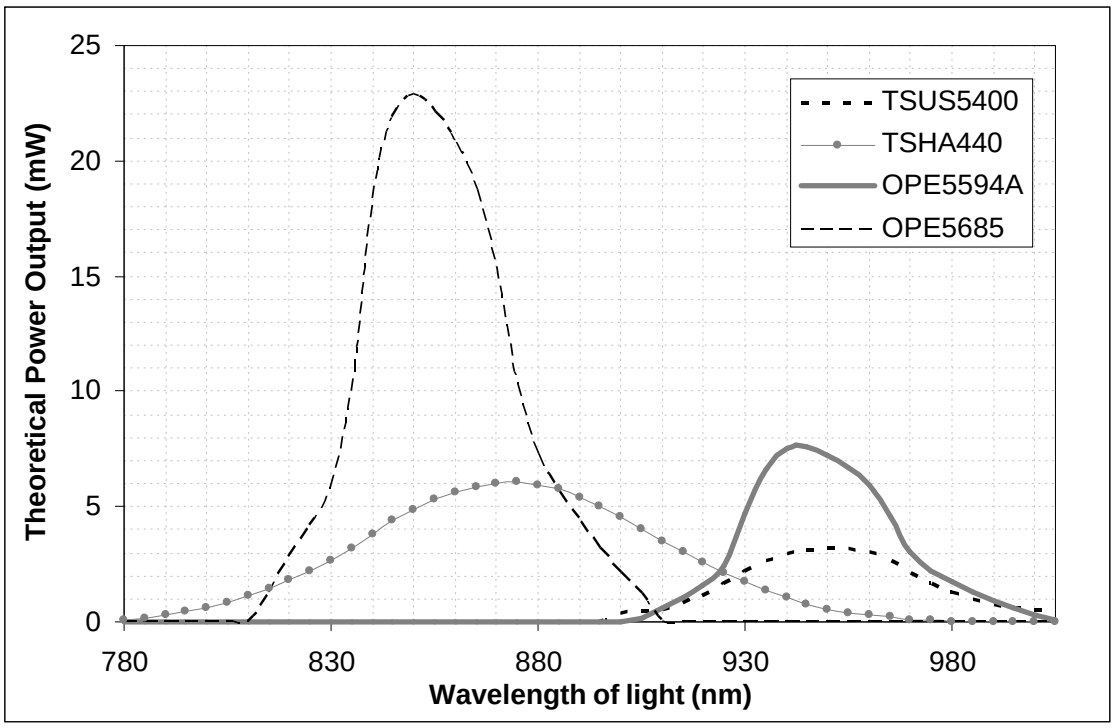


Figure 6-6 Theoretical spectral power curves of different LEDs

Since the photodiode that is used in the device also has varying sensitivity over the spectral range, the curves can be further moderated to determine the effect on allowed photocurrent. The plot of theoretical maximum current through the photodiode is given in Figure 6-7. It is

very similar in shape to the power curves of Figure 6-6, since the spectral sensitivity does not change dramatically over the output spectral ranges of the LEDs.

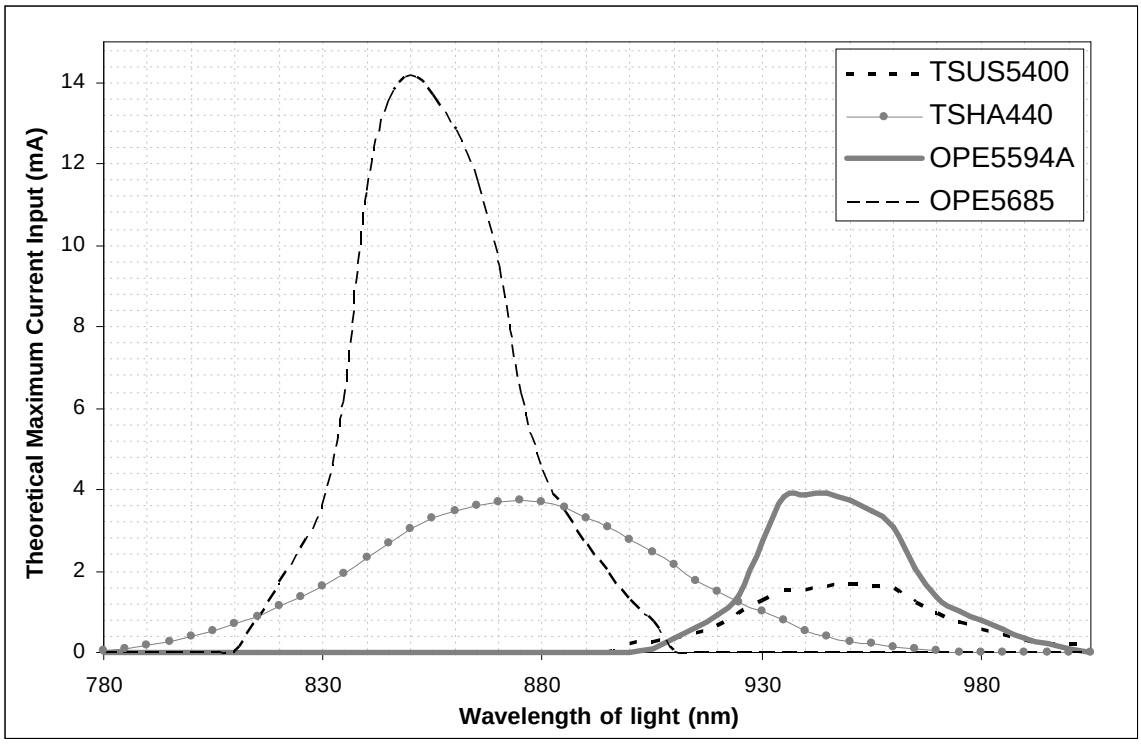


Figure 6-7 Theoretical spectral current curves produced by different LEDs in an SFH 203P

6.5.1 Relevance of Spectral Curves to the Sensors

So now that these curves have been established, we need to understand their relevance to the design of the sensor system. Suppose that the output voltage of the sensors, when applied to a certain sample correlated to a photocurrent of 10mA with OPE5685 activated, 2.5mA with TSHA440 activated, and less than 0.4mA for TSUS5400 and OPE5594A activated, we could say that something was absorbing a significant amount of the light in the spectral range of 900nm to 980nm. This can then be calibrated using a control sample (e.g. pure water for calibrating glucose solutions).

Also in the datasheets is a graph of the photocurrent and voltage as it varies with incident light intensity (lux) in the photodiode. Similar graphs are given for LEDs, though the units are watts. It is difficult to compare units of lux and watts in light intensity, since watts are a direct measure of power, and lux is based on how well our eyes can see the light, but we can derive from the graphs that the relationship between intensity of light and photocurrent is linear.

6.5.2 Initial Working Schematic

In this schematic diagram (Figure 6-8), the voltage source for the ADC and the OPAMP is external. This allows more control over the circuit than having them connected to one of the port lines.

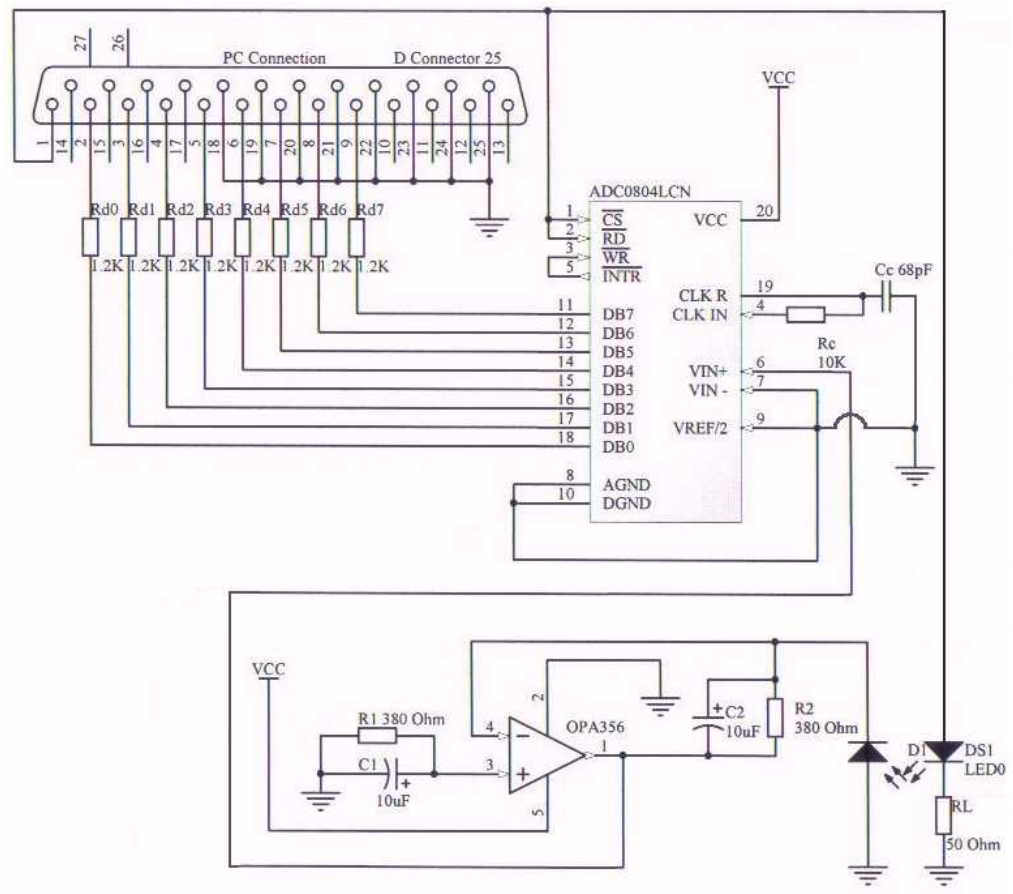


Figure 6-8 Schematic diagram of sensor circuit

6.6 Implementation and Testing

The circuit in Figure 6-8 was constructed and tested, but to limited success. It was observed that when powered up, the infrared LEDs flashed and then did not do anything. This of course is an obvious sign that the LED had been shorted, since the LED will only transmit light in a non-visible part of the spectrum, and a simple test of the voltage drop across it would have confirmed it.

It was not noticed that the op-amp would be acting as a voltage follower; there was no gain on it. So even if any IR light was transmitted it would not have been amplified. The amp was

only operating as a trans-impedance device, or taking a current from the photodiode and outputting a variable voltage based on the current level. Another problem could have been that some of the components were damaged while being soldered in place (I have not had a lot of experience with electronics and the surface mount op-amp looked doubtful).

The ADC chip appeared to be working with some success, though the digitally reported voltage was not accurate. For a voltage input to the chip of 0.18 V (tested with a simple multimeter), the output was a high level output on the data line 6. Digitally, the ADC was saying:

$$V_{analogue\ input} = (voltage\ ratio) \times (V_{CC} - V_{GND}) \quad \text{.....EQ. 6-11}$$

$$V_{analogue\ input} = \frac{\%\ 0100\ 0000}{\%\ 1111\ 1111} \times (5 - 0)$$
$$= 1.5V$$

Other pins like the clock circuitry of the chip were working as expected.

6.6.1 Circuit Re-design

A better way of testing the circuit and perhaps the method which should have been taken on in the start is to gradually build up the circuit and make sure each smaller system component is doing what it should. This is known as bottom-up testing. The circuit I began with in this process (basically an optocoupler) is shown in Figure 6-9.

The voltage drop across the LED is approximately 1.3 volts in normal operation. And an IR LED of this type needs a forward current of between about 10mA and 100mA. Then the resistor used for the circuit is chosen to produce a current of between 10mA and 100mA for a voltage drop of (5 - 1.3)V = 3.7V.

I had only 390Ω resistors to use for this resistance, so I paralleled three of them to produce a resistance of 130Ω. The current through the IR LED is then:

$$I = \frac{V}{R}$$
$$= \frac{3.7}{130}$$
$$= 28.5mA$$

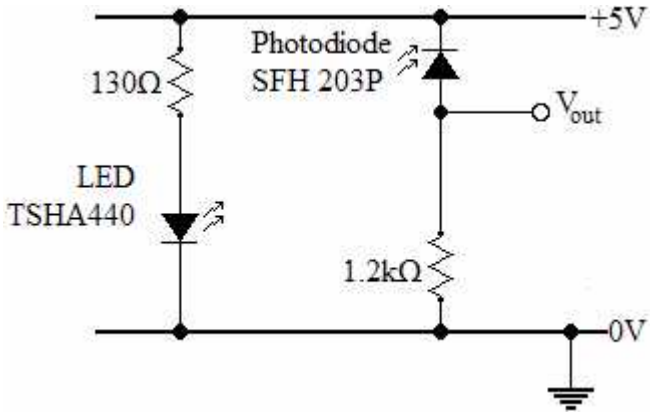


Figure 6-9 Photodiode test circuit

Using this circuit I was able to obtain voltage at the output which was dependent on the distance between the photodiode and the LED, so it appears the photodiode-LED combination was working. The resistance in series with the photodiode was chosen based on the spectral current curves. I initially used the TSHA440 LED in this circuit. It should have, according to the curves a maximum current across it of about 3.9mA. To obtain a maximum voltage of 4 volts then (to be read by an ADC), the resistance would be:

$$R = \frac{V_{out}}{I_{PH}} \quad \text{.....EQ. 6-12}$$

$$R = \frac{4}{3.9 \times 10^{-3}}$$
$$= 1.023k\Omega$$

The next largest value, 1.2kΩ was chosen.

But when the circuit was tested, the maximum value of V_{out} was 300mV, so the curves are not accurate for this particular diode combination. An increase in the value of resistance used destroyed the photodiode though, so the output voltage will have to be ranging from 0 to 300mV. Another interesting point is that when the OPE5685 was put into the circuit with the same resistance, less voltage was produced, so the TSHA440 appears to be more powerful.

6.6.2 Amplification

We would hope that the voltage at the output ranged higher than 300mV. So the next step is to amplify the voltage at the output. In the original circuit design (figure 6.8), the amplifier used was an OPA356. It was chosen for its high reliability and sensitivity, and low power consumption, as this may be an issue if the device is made portable. But it is a surface mount

component, which makes it difficult for development. A dual-in-line package is more suitable for this purpose as it can be tested on a breadboard. A cheap alternative for testing is the LM324N DIL package. It is able to operate on a +5V to 0V GND supply and can output voltages across the range from 0 to V_{CC} – 1.5V. It also contains 4 op-amps within the package, which allows for multiple-stage amplification if needed.

The op-amp is placed in the circuit as shown in Figure 6-10:

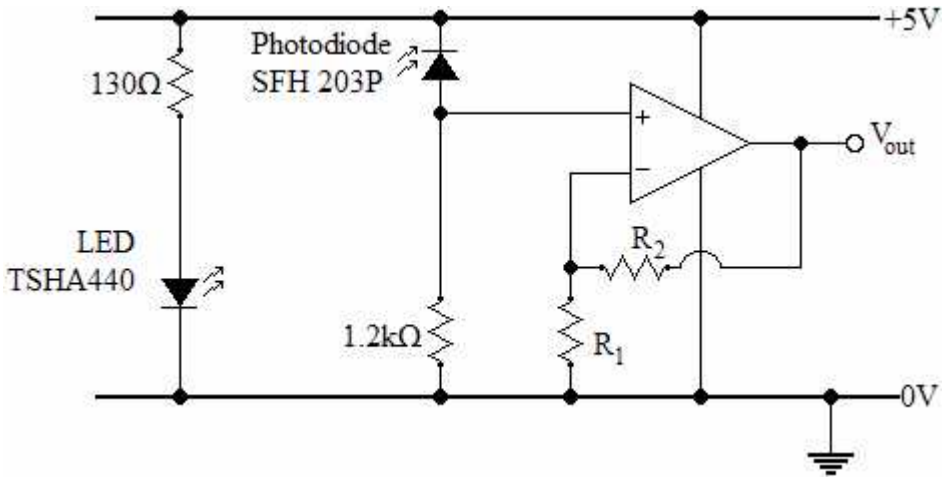


Figure 6-10 Photodiode test circuit with operational amplifier

In this layout, the op-amp is non-inverting, and in a series-shunt configuration. The gain of the amp, $A_V = V_{out} / V_{in}$, will be dependant on the resistor combination of R_1 and R_2:

$$A_V = \frac{V_{out}}{V_{in}} \quad \text{.....EQ. 6-13}$$

$$A_V = \frac{1+\frac{R_2}{R_1}}{1+\frac{1}{A_{V(open-loop)}}\left(1+\frac{R_2}{R_1}\right)}$$

$$= \frac{1+\frac{R_2}{R_1}}{1+\frac{1}{100000}\left(1+\frac{R_2}{R_1}\right)}$$

$$A_V \approx 1+\frac{R_2}{R_1} \quad \text{.....EQ. 6-14}$$

If we are getting 300mV at the input to the op-amp, and the maximum voltage swing of the op-amp is 0V to (5 – 1.5)V = 3.5V, then the desirable voltage gain would be:

$$A_V = \frac{V_{out}}{V_{in}}$$
$$= \frac{3.5}{300 \times 10^{-3}}$$
$$= 11.7$$

$$\therefore \; 11.7 = 1 + \frac{R_2}{R_1}$$
$$R_2 = 10.7 R_1$$

A suitable resistor combination would be R_1 = 1kΩ and R_2 = 10kΩ.

6.6.3 Connection to a PC

An aim of the original design was to relay the measurements of the device to a personal computer in parallel digital form. To achieve this, the ADC0804LCN is used. This analogue to digital converter has been discussed in previous sections, but not in adequate detail. In the initial testing of the circuit, to relieve the complexity of connecting to a PC, the digital output is displayed on 8 simple red LEDs.

Without the connection to a PC or some sort of microcontroller, the ADC will operate in the free-running mode. This just means that chip-select, read write lines and clock signals are hard wired to a fixed state.

In the active state, the RD (read) and CS (chip-select) lines are held low. In the test circuit, these two lines were just tied to ground or 0V. The WR (write) and INTR (interrupt) lines are tied together so that the chip is constantly telling itself to sample each time the clock circuitry pulses. To begin sampling, the chip needs an active low pulse on the WR line, so the circuit has a normally-open switch connected from WR to ground.

In the previous circuit, $V_{ref}/2$ was wired to ground. This is actually incorrect, as it would have told the chip the input voltage range was from 0V to 0V. Actually the range of the output of the op-amp is from 0V to just over 3V, so the $V_{ref}/2$ value should be approximately 1.5V. I decided to set the $V_{ref}/2$ to 1.6V. This can be obtained by using a voltage divider circuit:

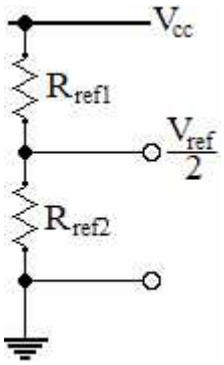


Figure 6-11 Voltage divider for ADC0804LCN reference voltage

$$\frac{V_{ref}}{2} = V_{CC}\left(\frac{R_{ref2}}{R_{ref1}+R_{ref2}}\right) \quad \text{.....EQ. 6-15}$$

$$1.6 = 5\left(\frac{R_{ref2}}{R_{ref1}+R_{ref2}}\right)$$

$$1.6R_{ref1} + 1.6R_{ref2} = 5R_{ref2}$$

$$R_{ref2} = 0.471R_{ref1}$$

$$\therefore R_{ref1} = 10k\Omega,\ R_{ref2} = 4.7k\Omega$$

Capacitors are also used on some of the pins that are going to ground, to eliminate the effect of voltage or current spikes. A schematic of the circuit as implemented on a PCB is given in Figure 6-12.

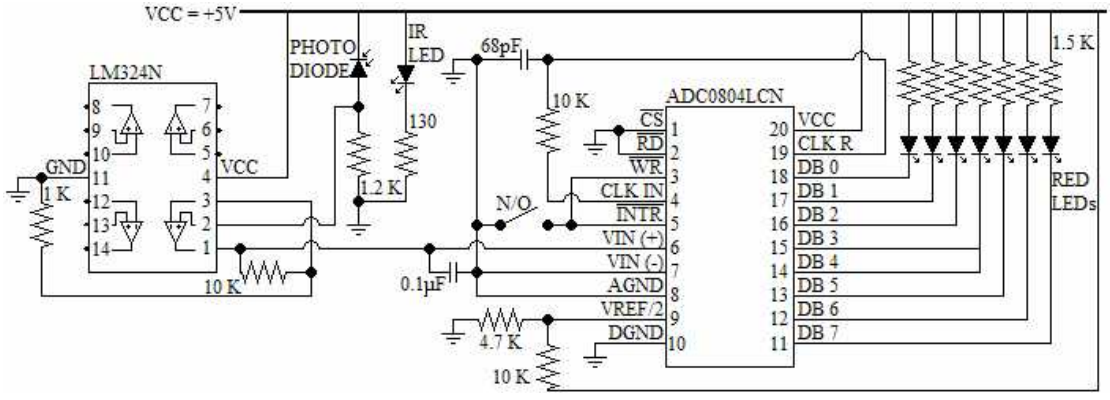


Figure 6-12 Photodiode test circuit

6.7 Light Diffraction

Analysis of wavelength via the spectral curves is one method to isolate peak absorbance wavelengths, and may be unreliable, as shown through testing in the previous section. The

spectral curves for each LED can vary, meaning that each would need to be calibrated before use – a very tedious and expensive process. Theoretically, with enough different LEDs it would be possible to use the spectral curves.

A more direct and tried method though is using a special light-diffracting lens to isolate small parts of the spectrum. An example of a light-diffracting material is the plastic layer of a compact disc. If a white light is shone on a CD, the reflected light is separated into its spectral components, and an observer can see bands of different colours. Another common example is rainbows produced by water particles in the air.

Diffraction lenses are available that work on the spectral range from 400nm to 1500nm, so there is definitely an application for them in measuring wavelength of light for the near-infrared range. And their basic physical properties allow easy 'tuning' as required.

6.7.1 Application of the Diffraction Grating

The effect of a diffraction grating on a light source is illustrated in Figure 6-13.

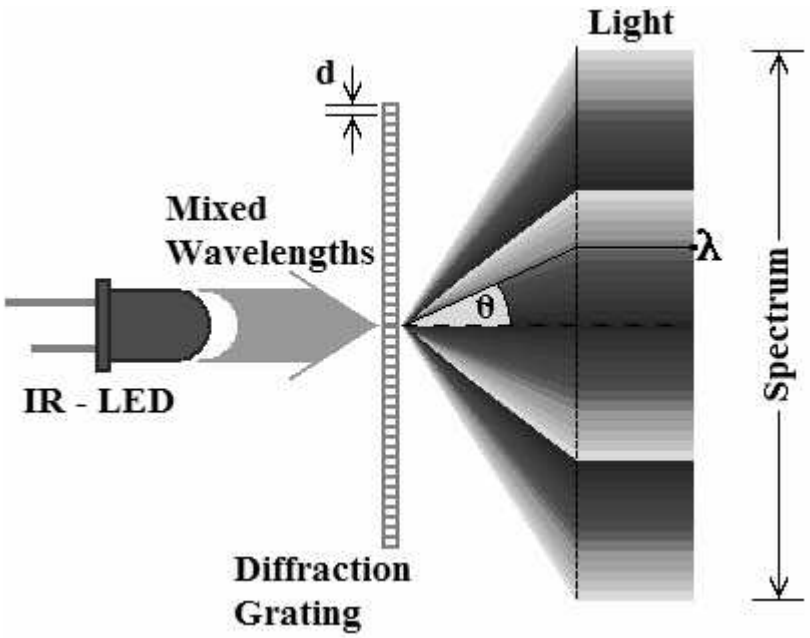


Figure 6-13 Diffraction grating illustration

In the illustration, *d* is the distance between etched lines in the grating, θ is the angle of the measured light from the normal direction and λ is the wavelength of light at that particular angle. The other important parameter is *m,* which is the order of the grating, or basically a

measure of the number of non-negligible bands of similar light wavelength. The equation that represents this is:

$$\theta = \sin^{-1}\left(\frac{m\lambda}{d}\right) \quad \text{.....EQ. 6-16}$$

Given the specifications of the diffraction grating, a sensor can be placed to measure the intensity of a particular light wavelength. To isolate the wavelength, the light could be made shine through a slit in a material that blocks out near infrared, as shown in Figure 6-14. The position of the slit can then be controlled to tune the sensor into a particular wavelength.

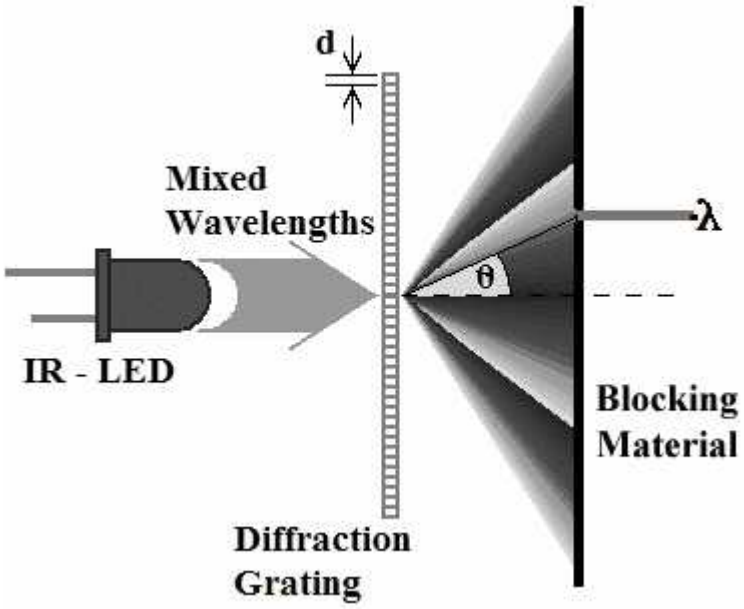


Figure 6-14 Use of a blocking material to isolate particular wavelengths

As explained previously, a common compact disc is an example of a diffraction grating. A compact disc has track spacing (*d*) of 1600nm, and operates with a light wavelength of 780nm. So can a CD be used as an experimental diffraction grating for this project?

Figure 6-15 shows the theoretical angular response to wavelength of a CD operating as a diffraction grating ('*m*' is the wavelength order of the light):

According to the figure, as long as light is not transmitted at lower wavelengths, (which it would not with the LEDs selected earlier), it will be possible to isolate a particular wavelength. What this wavelength actually is will depend on the type of diode and the actual physical properties of glucose.

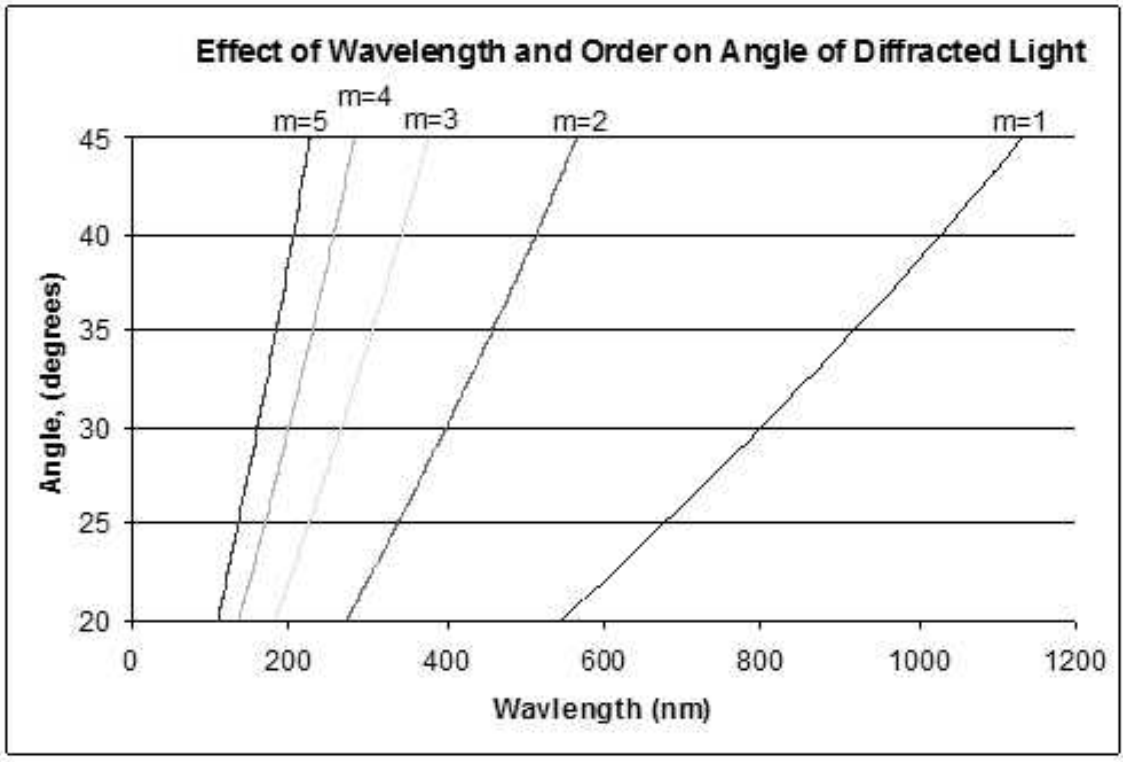


Figure 6-15 Angle of diffracted light in a compact disc.

For the purposes of testing, the device should be able to be tuned.

6.7.2 Refractive Index of Glass and Test Substance

The diffraction grating has a effect on the direction of light it lets through, but we should also expect the test substance and the glass vessel holding the test substance to have an effect. This effect can be quantified by looking at the refractive indexes of the materials. Basically, the light will be refracted in a manner according to Snell's Law:

$$n_1 \sin(\theta_1) = n_2 \sin(\theta_2) \quad \text{.....EQ. 6-17}$$

Where n_1 and n_2 are the refractive indices of the two materials that light is passing through (e.g. air to glass, glass to water), and θ_1 and θ_2 are the angle of incidence and angle of refraction respectively.

A way to avoid problems can be derived from equation 6-17. If the angle of incidence is 0, the angle of refraction is also zero, regardless of the refractive index of either material. So in constructing test equipment, this will need to be kept in mind to avoid extra complexities.

6.8 Conclusion

Three of the basic light-dependent components have been investigated in this chapter; photocells, phototransistors and photodiodes. It was discovered that photodiodes would give the most accurate and linear response to a level of light intensity.

Photodiodes have been investigated in more detail and ideal responses to varying light wavelength have been determined. A circuit has been designed and built based on measuring the current produced in a photodiode due to incident light, ready to be used in the testing stage.

Fine tuning of light frequencies using diffraction gratings has been also investigated.

Chapter 7 : TESTING FOR GLUCOSE

7.1 Introduction

A basic circuit has been designed and constructed, as detailed in the previous chapter. Experiments can be conducted using this circuit, into the ability to find glucose in various test samples. The methods used to test for glucose are similar to those experiments conducted by researchers at the Tianjin University, as described in section 4.2.

The tests involve dissolving specific amounts of glucose powder into water. A de-ionised water sample will be optimum for the control for this experiment, as all other factors could be eliminated. However due to issues with availability, ordinary tap water was used. It is hoped that results will show a relationship between the amount of dissolved glucose and the amount of absorbed light at the four different available wavelengths.

Another test that would have been carried out if there were positive results from the first test would involve using a fluid, similar in its physical properties to human blood. Like the first test, a "pure" sample of the synthesised blood will be used as a control, and specific amounts of glucose will be added to the solution to find a relationship, if any, between absorbed light and glucose concentration. Because the test fluid will only chemically resemble human blood, there should not be need for ethical concern.

A third test, if there had been positive results from the first two tests, and if time allowed, would have involved using live subjects. The Tianjin study did not go so far as to test living flesh, though it did use human blood serum. In their tests, the light path was only 1mm, so there may not have been enough power for in-vivo tests. Obviously, there is an ethical responsibility when dealing with real people in this manner. I would need to take extra precaution when dealing with diabetic patients to minimise any effect I may have on them.

This is for both the health safety of the diabetic and the legal safety of myself and the university. To ensure safety I would need to consult medical staff at the hospital and have them explain to me the best practices for patient interaction, and also request their supervision during any testing procedures. Since positive results were not obtained however, I can only offer this as recommended further work.

7.2 Simple Glucose Solution A

The aim of this test is to determine the relationship if any between glucose concentrations in a pure glucose–H_2O solution and output voltages from the test device designed in Chapter 6.

7.2.1 Method

The circuit used for testing the glucose solutions is a reduced form of Figure 6-12 (Figure 7-1):

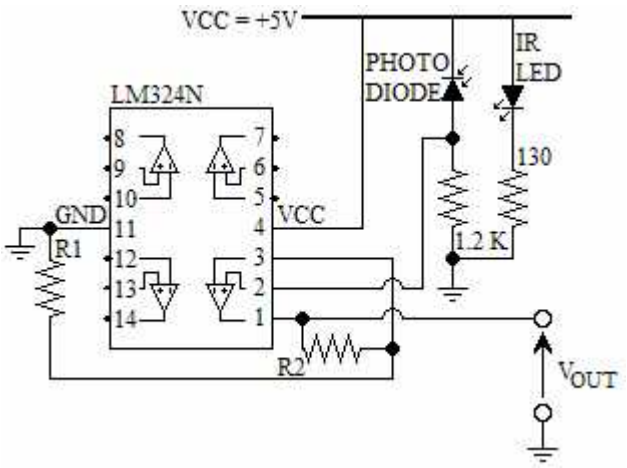


Figure 7-1 Test circuit

For the first set of results (set **A**), the R_1 and R_2 resistor values were selected as 1K and 10K respectively. Because the op-amp is connected as non-inverting, the gain is:

$$A_V = 1 + \frac{R_2}{R_1}$$
$$= 1 + \frac{10K}{1K}$$
$$= 11$$

In circuit, the gain is actually just less than 11, about 10.8. The exact is not important for the purposes of this experiment, just that it is consistent for different voltage inputs.

For the first test, the glucose solutions were made by dissolving pure glucose powder in a half cup of tap water. An assumption is there is no impurity in the tap water great enough to affect measurements. The amount of glucose added to the water was not precisely measured, and is given in the results as 'teaspoon' and 'dessertspoon' measurements. The solutions were fed down a 3mm poly-vinyl pipe, three times for each solution, and the voltage was measured at the output of the op-amp each time. Figure 7-2 is a photo of this experiment.

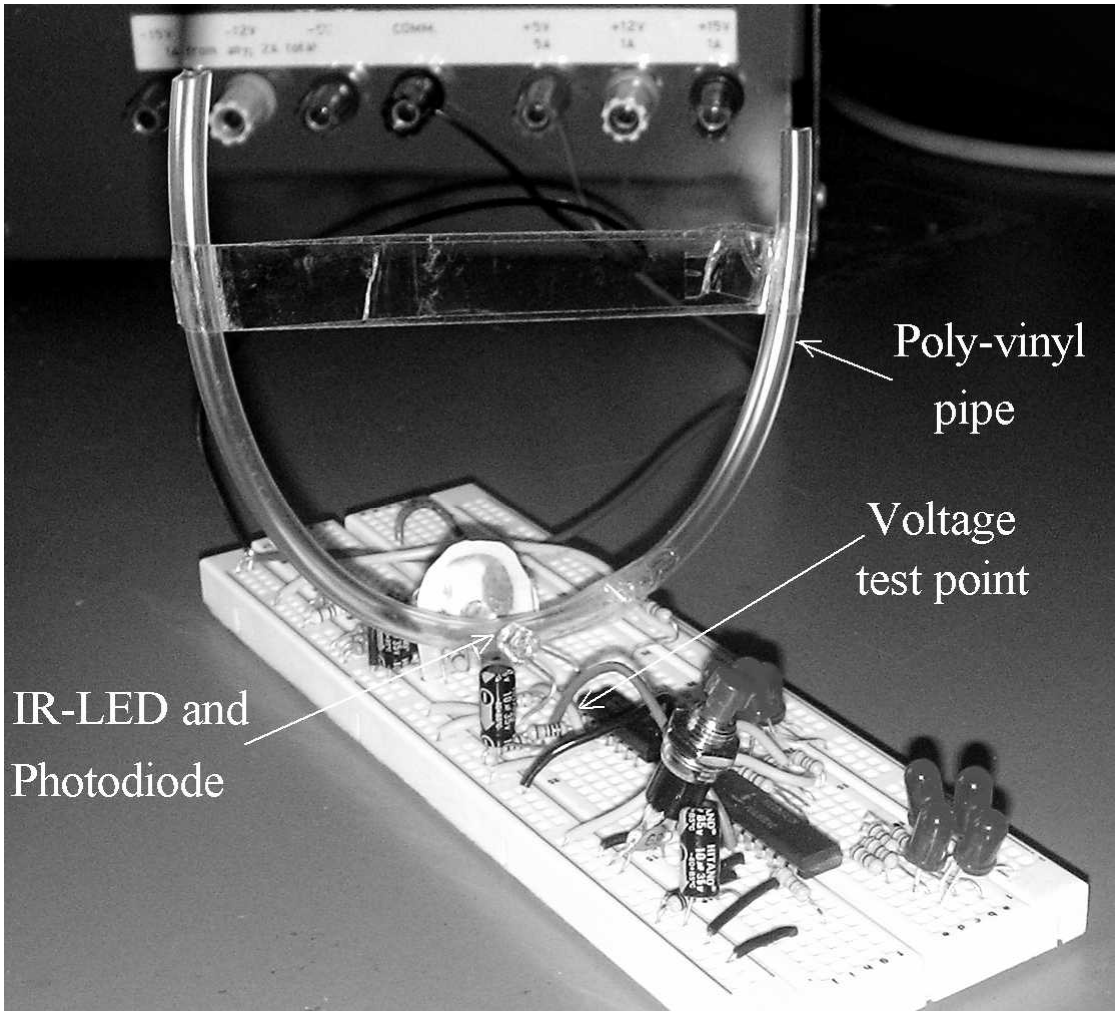


Figure 7-2 Photo of test A

7.2.2 Results

The test was repeated for increasing levels of dissolved glucose. Amount of glucose added is not linear or even measured accurately, but there is a trend shown for increasing levels of glucose. Data 1, data 2 and data 3 represent the three times each solution was tested. Data 3 may be the more reliable measurement, as it was conducted last, giving the glucose more time to thoroughly dissolve. Figure 7-3 is a plot of the results.

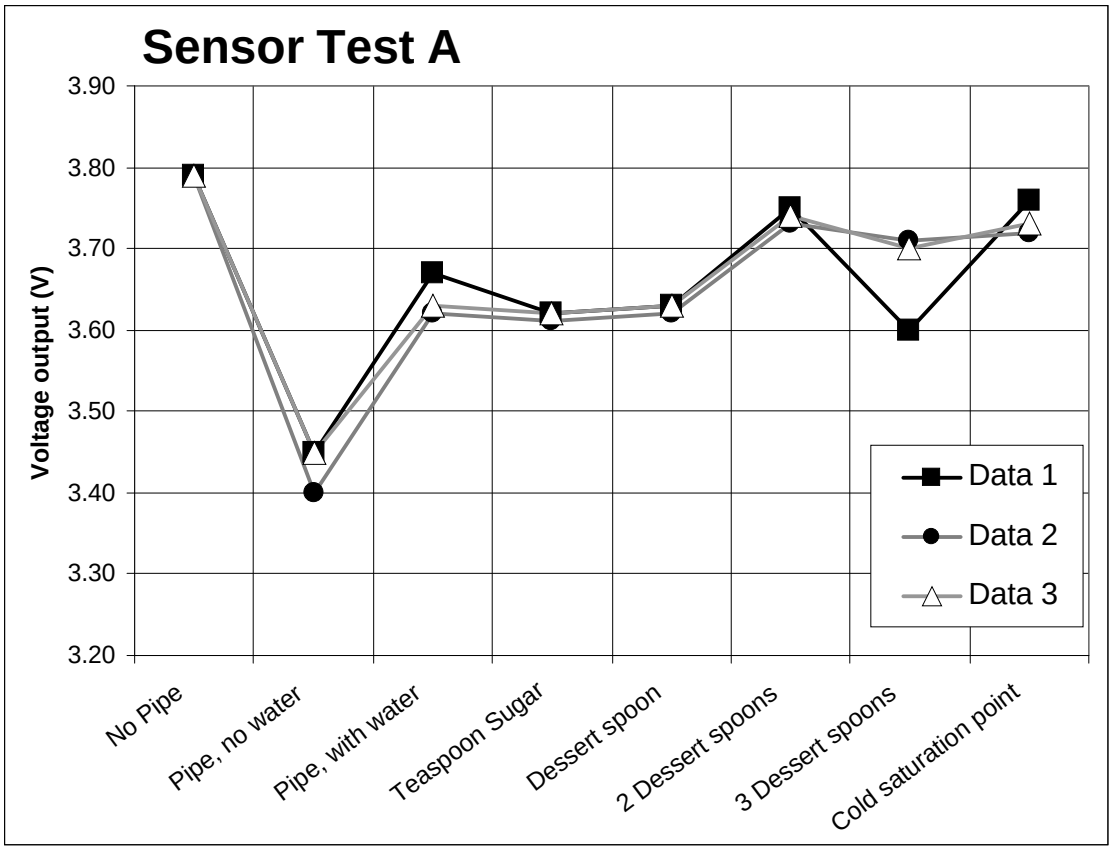


Figure 7-3 Results of test A

7.2.3 Conclusion / Discussion

There was some trouble with an air-lock in the pipe; I had to blow through it to get the solution in the right place. Fortunately the solutions being tested are not harmful chemicals.

Results obtained showed a trend in measurements as glucose was added. The amount of glucose added was probably not well representative of blood; in blood, the amount of sugar is much less than this. A healthy level is about 100mg/dL (Table 2-1), whereas what I added would be at least ten times this value. Around 2 to 3 dessertspoons had a very sweet taste. The accuracy of measurements could be improved with higher resolution on the multimeter.

The idea of using the infrared light was to measure how much was absorbed when passed through a test substance. An expectation was that the absorption would increase as more glucose was added. But actually, as more glucose was added, the voltage increased, apparently indicating that the absorption had decreased. If this was the case though, how could the increase in voltage (lower absorption) when water was added be explained?

Another more likely explanation is that the refractive index of a glucose solution is more similar to that of the polyvinyl pipe than air or plain water. This would cause less light to be diffracted away from the photodiode. It was noticed that the direction the IR-LED was pointing in relation to the photodiode was very significant in the measured voltage at the output, so any refractive effect would play an important part.

Just based on this first test, I would conclude that the components used are not really capable of determining glucose concentration in the blood.

7.3 Simple Glucose Solution B

The aim of this test is to verify the results obtained in test A.

7.3.1 Method

Sensor design in this test is similar to the previous; except that R_1 and R_2 have been changed to 1.2kΩ and 10kΩ respectively (refer Figure 7-1). This reduces the gain in the op-amp to 9.33 to keep the output voltages below two volts. This just allows more accuracy as the multimeter can display voltages in millivolts (10^{-3} V) rather than centivolts (10^{-2} V) below two volts. Also changed is the infrared LED. In the first test, only the OPE5594A LED was used. In this test, results are given for the OPE5685 LED also. The OPE5685 is a more powerful LED than the OPE5594A.

In this test, glass slides are used instead of the tube to eliminate possible effects of refraction; the glass slides being flat may be less likely to bend the light. To prepare a test sample, the glucose was mixed thoroughly with water in a half cup of water (careful to make sure it totally dissolves). Again, the quantity of glucose is not really accurate; the rest of the experiment is not yet accurate enough to warrant measuring exact weights of glucose powder.

Red food colouring is added to the solution this time to see if it had any effect. One teaspoon of glucose is added at a time to the solution, and the measurement of voltage is taken five times for each teaspoon. A photo of the test is given in Figure 7-4.

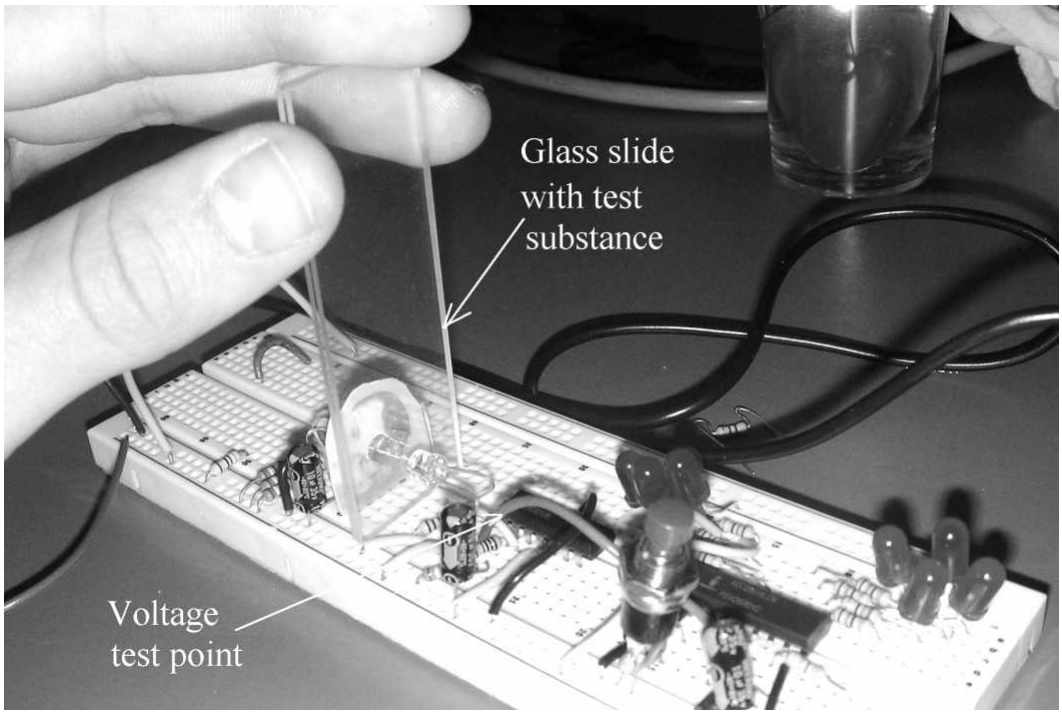


Figure 7-4 Photo of test B

7.3.2 Results

The voltage measurement was very sensitive to the IR-LED and photodiode being bumped, so rather than plotting the voltages output, the difference between voltage measurement with the slide and immediately after with the slide taken out is plotted. Results are shown in Figure 7-5 and Figure 7-6.

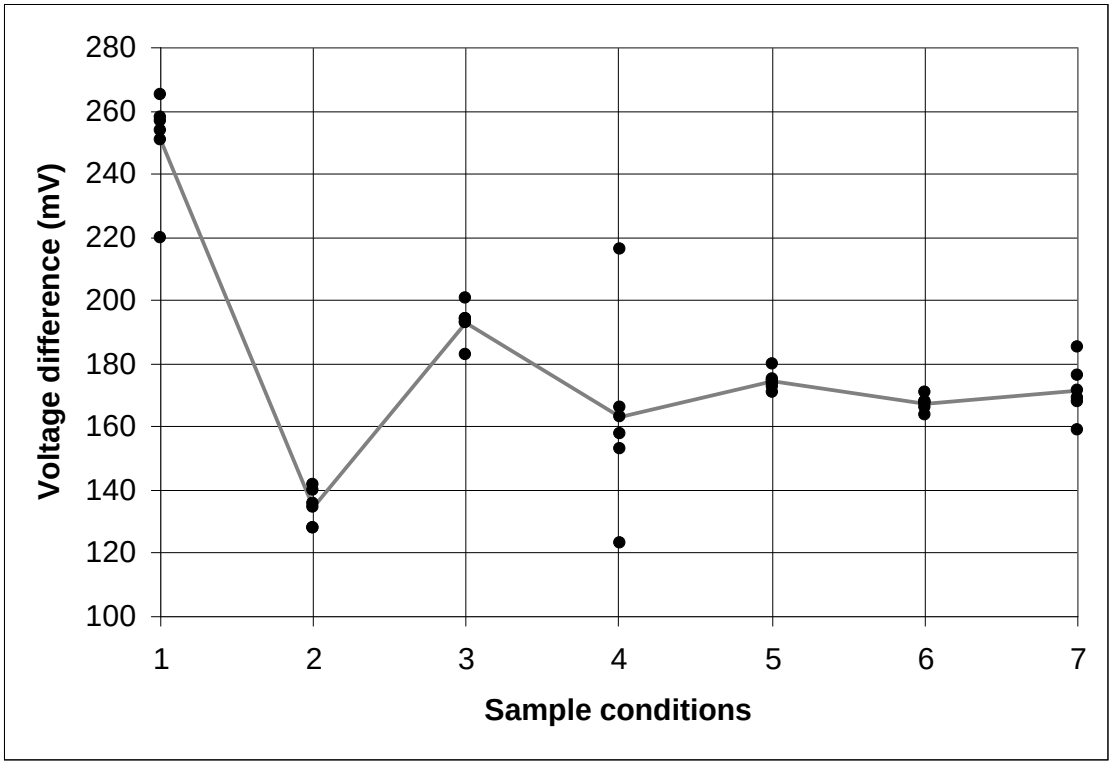


Figure 7-5 Results of test B – OPE5594A

Table 7-1 Explanation of Sample conditions for Figure 7-5

	SAMPLE CONDITIONS
1	Empty slides (no liquid)
2	Water added to slides
3	2 Drops of red food colouring added
4	One tsp glucose added (approx. 3000 mg/dL or 167 mmol/L solution)
5	2 tsp glucose added (approx. 6000 mg/dL or 333 mmol/L solution)
6	3 tsp glucose added (approx. 9000 mg/dL or 500 mmol/L solution)
7	4 tsp glucose added (approx. 12000 mg/dL or 667 mmol/L solution)

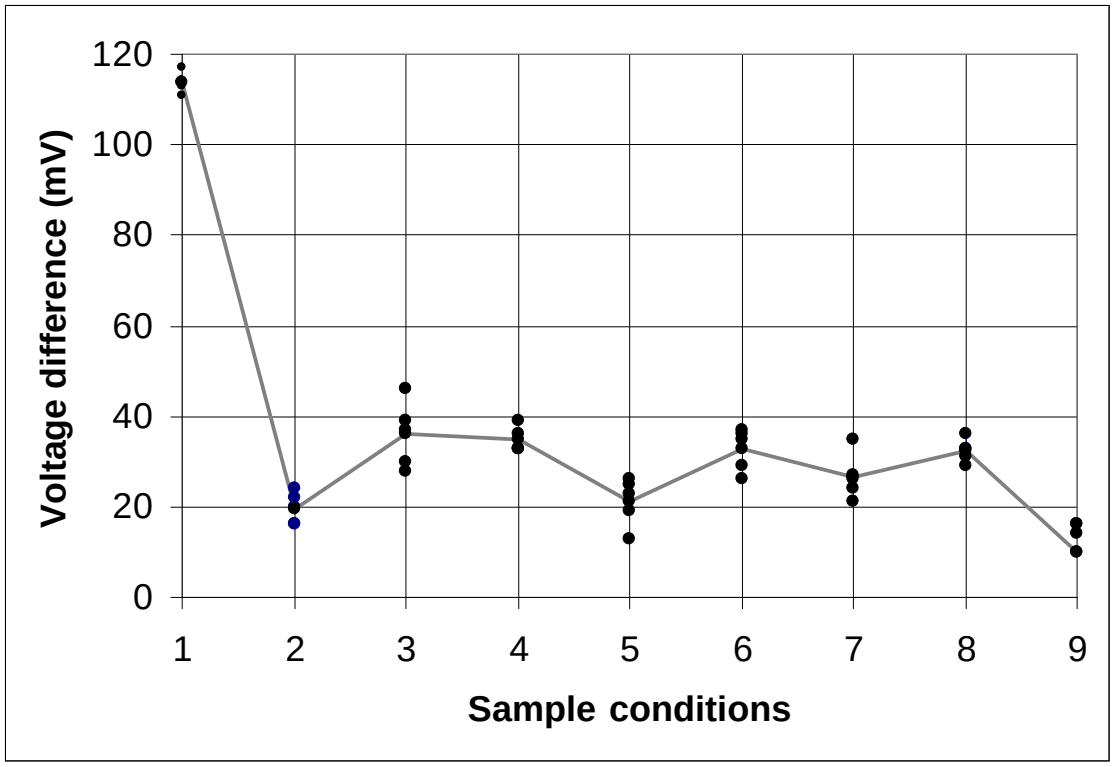


Figure 7-6 Results of test B - OPE5685

Table 7-2 Explanation of Sample conditions for Figure 7-6 and Figure 7-7

	SAMPLE CONDITIONS
1	Empty slides (no liquid)
2	Water added to slides
3	Half tsp glucose added (approx. 1500 mg/dL or 83 mmol/L solution)
4	One tsp glucose added (approx. 3000 mg/dL or 167 mmol/L solution)
5	1.5 tsp glucose added (approx. 4500 mg/dL or 250 mmol/L solution)
6	2 tsp glucose added (approx. 6000 mg/dL or 333 mmol/L solution)
7	2.5 tsp glucose added (approx. 7500 mg/dL or 417 mmol/L solution)
8	3 tsp glucose added (approx. 9000 mg/dL or 500 mmol/L solution)
9	Cold water saturation (will not dissolve any more glucose)

7.3.3 Conclusion / Discussion

Similar to the first test, the absorbance apparently reduced when water was added to the slides. There is probably some reflectance happening when there is an air gap between the slides, which doesn't happen when water is added, because refractive indices are much closer together.

There is an affect on voltage from the red colouring, more of an affect than glucose. Keeping in mind the spread of data points in the graph, there still is a faint trend as the amount of glucose increases that more light is getting through.

The OPE5685 was obviously more powerful. A plot of the photocurrent produced, based on the voltage for the two diodes is given in Figure 7-7. In this test, the distance between LED and photodiode was 2.5mm for the OPE5594A LED and 6mm in the OPE5685 LED.

In terms of the purpose of this sensor, the trend is not really definite enough. The amount of glucose added is much higher (as much as ten times) than what should be present in the blood. The test slides are about as plain as possible for this sort of test, but rotating them only slightly has a significant effect on voltage output. The sensitivity of the LED and photodiode being bumped out of alignment also has a very significant effect on measurements (i.e. 10% error for very slight alignment change <<1mm). And a test in the body will almost certainly have many other aspects to affect measurements. Because of these things, it appears that the components used are not capable of reliable glucose measurements.

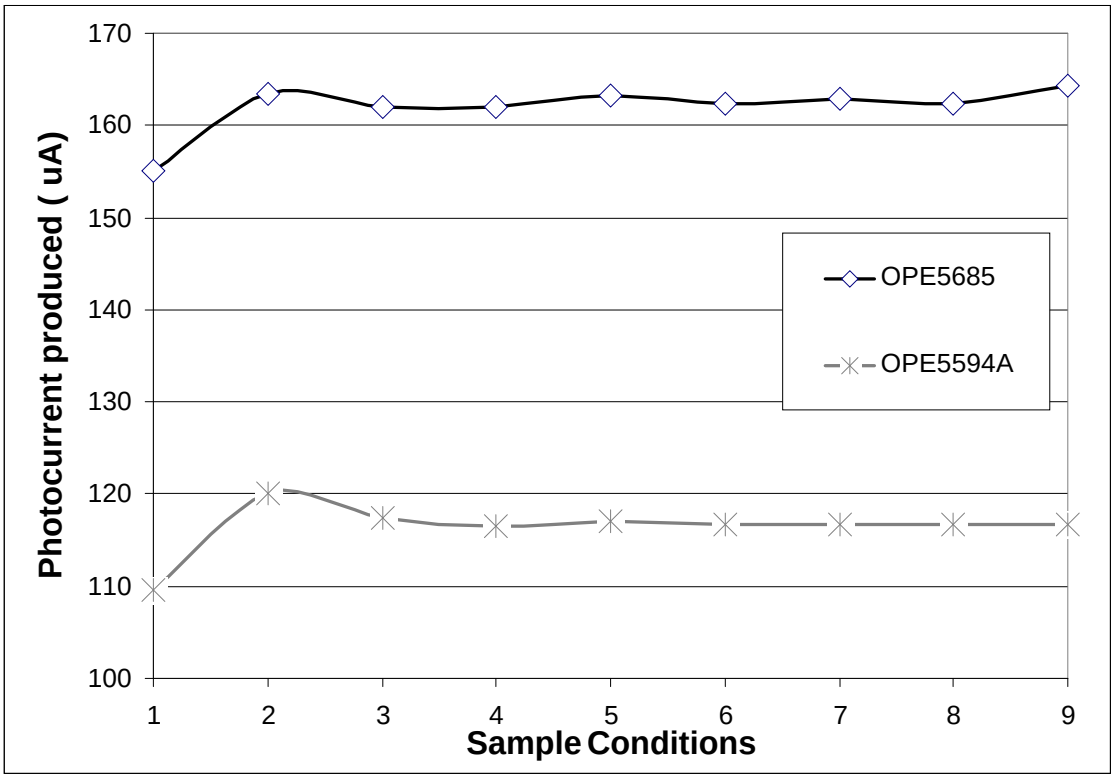


Figure 7-7 Estimated photocurrent produced in the test

Chapter 8 : CONCLUSIONS AND RECOMMENDATIONS

8.1 Introduction

This chapter will firstly give an overview of the achievements of this project. A further discussion on the results of experimentation is given, to relate the results to previous research in the area of glucose sensors, and determine the prediction accuracy of results.

8.2 Achievements of this Project

- Background research into the disease diabetes. I have found that there is a definite need for a non-invasive glucose sensor. Glucose is a vital source of energy for our bodies, which diabetics metabolisms have less ability to control. Diabetics need to artificially control their glucose levels through dietary supplements and insulin treatments, and hence need to know what their current blood glucose levels are. Statistics show that a significant proportion of the population of Australia suffer from the disease, and based on current trends, that proportion may increase in the future.
- Research into different types of sensors in development and in present use, including some non-invasive sensors. The result of this research is the awareness of a range of different indicators of glucose levels, including the chemical reactance to specific enzymes, the thermal emissions of glucose in the body, and the absorbance and reflectance properties of glucose molecules to infrared light.
- Development of conceptual designs for a sensor device based on the absorbance properties in the near-infrared range.
- Investigations into the viability of light-producing and light responsive components and development of a test circuit.

- Experimentation using the aforementioned test circuit to find any relationship between concentrations of glucose in a solution and the amount of light absorbed by that solution.

8.3 Discussion on Experiments

It appeared from the results of the experimentation that there was more of a refractive effect than absorbance. The addition of glucose to water allowed more light through.

The greatest limitation to the experimentation in this project was the inability to scan across the infrared spectrum for absorption peaks.

To determine whether there was any value to the testing carried out in the previous chapter, the results can be reviewed in terms of the prediction accuracy models reported in section 4.2:

$$I = I_0 e^{\left(-\sum_{i=1}^{n} a_i(\lambda) c_i L\right)}$$

$$\frac{I}{I_0} = e^{\left(-\sum_{i=1}^{n} a_i(\lambda) c_i L\right)}$$

$$-\ln\left(\frac{I}{I_0}\right) = \sum_{i=1}^{n} a_i(\lambda) c_i L$$

In each test, there is only one substance tested, so $n = 1$, hence the equation is:

$$-\ln\left(\frac{I}{I_0}\right) = a_i(\lambda) c_i L$$

$$a_i(\lambda) = \frac{\ln\left(\frac{I_0}{I}\right)}{c_i L} \quad \text{.....EQ. 8-1}$$

The intensities I_0 and I produce photocurrents in the diode which vary in a linear manner (refer to equation 6-6 in section 6.4). In the circuit this current causes a voltage across a 1.2kΩ resistor (Figure 6-9) which is also a linear relationship. This means that:

$$I = \frac{i_P}{S_\lambda}$$

$$= \frac{V}{1200.S_\lambda}$$

So an equivalent equation to equation 8-1 which uses the format of results from testing is:

$$a_i(\lambda) = \frac{\ln\left(\dfrac{\dfrac{V_0}{1200.S_\lambda}}{\dfrac{V}{1200.S_\lambda}}\right)}{c_i L}$$

$$a_i(\lambda) = \frac{\ln\left(\dfrac{V_0}{V}\right)}{c_i L} \quad \text{.....EQ. 8-2}$$

Equation 8-2 is applied to the results of the Simple Glucose Solution B test:

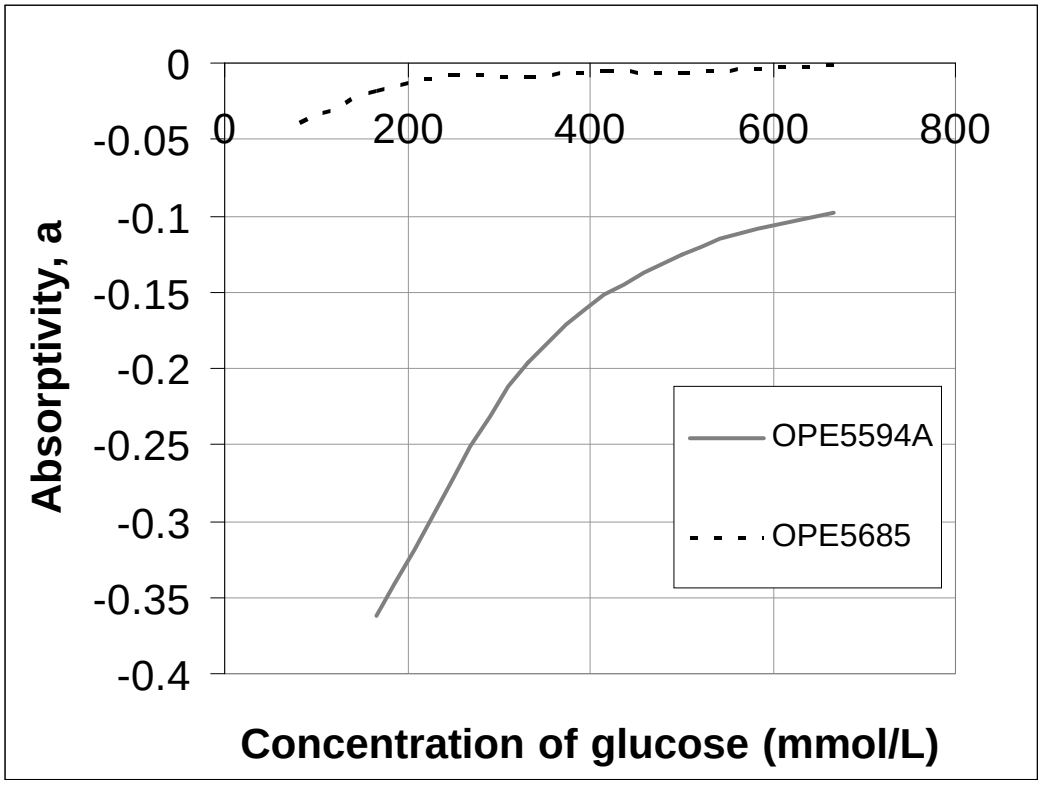


Figure 8-1 Absorptivity a function of concentration?

If the results of the test are of value, then $a_i(\lambda)$ should be constant for a particular LED over a range of different concentrations when light is passed through glucose (because a_i is a function of wavelength). The response of a_i does appear to be dependant on wavelength.

Errors could be caused by:

- Errors in taking measurements. The circuit was very sensitive to being bumped, though care was taken to be consistent in the experimentation. Repeated

experiments with a more rigid test assembly (experiments were carried out with a breadboard) could improve results.

- The glucose samples used in the experiments were very thin – the solution was pressed between glass slides. Lack of definite trends in the results could be due to there being not enough glucose to absorb light.
- In the experiments, it was expected that the incident light energy would reduce when more glucose was dissolved, indicating a light-absorbing tendency. The results showed the opposite. This could be because the LEDs did not project a peak absorbance wavelength for glucose, or that they did not only project a peak wavelength. The LEDs used will project light at wavelengths over a 50nm range, the peak could be within this range, but if the rest is getting through un-absorbed the peak would be hidden. Considering that the whole of the visible range of light wavelength are between 400 nm and 700 nm, 50nm is fairly broad. The response could be improved with diffraction gratings, or different light sources.

8.4 Further Recommended Work

There is a lot of work that could be done on this project topic in the future. Nothing very conclusive can be drawn from this project, only that I haven't developed a non-invasive way to detect glucose yet.

I have established that the frequencies I tested did not indicate the characteristic absorbance peaks of glucose solutions. Given more time, I would have tried using LEDs and photodiodes rated at other peak wavelengths.

It would also be valuable to find a way to scan through the near-infrared range to find out where absorbance peaks actually lie. If a spectroscope was available, testing should be done to find them.

The project could be advanced a lot further if a characteristic curve of glucose solution reaction to light was found. I did not find one in any of the journal articles used for this project, or anywhere else in the texts I researched. But some of the articles did mention about signal to noise ratios, so they must have developed a characteristic curve or equivalent data through experimentation. It would be a good idea to get in contact with these people and ask them whether they could send any of that information.

Some of the other methods of testing for glucose could also be researched, such as impulse response to light, and thermal emission measurements. Incorporating more than one of these methods into the same device could be a way to ensure the results obtained indicate glucose concentrations.

8.5 Conclusion

This project has introduced many of the concepts used in monitoring glucose levels and present research into the area of non-invasive monitoring. Based on this research, it was decided that near-infrared light had a potential to be used for non-invasive monitoring of blood glucose levels. Through the designs and experimentation developed in the project, I have found that there could be a way to use near-infrared light as a means of determining a person's glucose levels, though I was not able to produce such a device myself. I believe, given more time and other resources, it is possible to realise the goal of non-invasive monitoring, and when that happens, the benefits for diabetics and health-care professionals will be immense.

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Appendix A: PROJECT SPECIFICATION

University of Southern Queensland
FACULTY OF ENGINEERING AND SURVEYING

ENG 4111/4112 Research Project

PROJECT SPECIFICATION

FOR: **Ross Donald GILLIES**

TOPIC: *NON-INVASIVE MONITORING OF BLOOD GLUCOSE LEVELS IN PEOPLE WITH DIABETES*

SUPERVISORS: Dr Selvan Pather

ENROLMENT: ENG 4111 – Semester 1, ONC, 2005
ENG 4112 – Semester 2, ONC, 2005

PROJECT AIM: This project aims to investigate the methods available for the non-invasive monitoring of blood glucose levels, and to determine the viability of a blood glucose sensor unit.

PROGRAMME: Issue B, 24th May 2005

1. Research briefly the diabetic condition.
2. Research the different types of medical sensors available at present, if they exist what they are able to measure and the format of their output.
3. Perform testing on glucose solutions (possibly in the body) and measure the output signal.
4. Construct empirical models of blood glucose based on the testing.
5. Design control systems based on the empirical models that may be later implemented on a PC or on an embedded system.

AS TIME (and positive investigation results) PERMITS:

1. Implement the glucose sensor as an embedded system.
2. Test the system with clinical trials.

AGREED:

_____ (Student) _____, (Supervisor)
___/___/_____ ___/___/_____

Appendix B: MOTOROLA M68HC908 PROGRAMING

(Refer to section 5.4)

Programming a line of Flash memory in a Motorola MHC12 microcontroller

```
FLPROG      LDA         #%0000 0001
            STA         $FE08           Enable programming
            LDA         $FF7E           Read from FLASH block protect

**********Write any data to FLASH address in desired row**********
DELAY10     LDX         #$14            10 Microsecond delay
LOOP1 DECX
            BPL         LOOP1       Loop 20 times
            LDA         #%0000 1110
            STA         $FE08           Enable high voltage (HVEN)
DELAY5      LDA         #$0A            5 Microsecond delay
LOOP2 DECA
            BPL         LOOP2       Loop 10 times

**********Write data to FLASH address**********
DELAY30     LDA         #$3C            30 Microsecond delay
LOOP3 DECA
            BPL         LOOP3       Loop 60 times
            LDA         #%0000 1000
            STA         $FE08           Clear PGM bit
DELAY5      LDA         #$0A            5 Microsecond delay
LOOP4 DECA
            BPL         LOOP4       Loop 10 times
            LDA         #%0000 0000     Disable high voltage
DELAY1      LDA         #$0A            1 Microsecond delay
LOOP5 DECA
            BPL         LOOP5       Loop 2 times
            RTS
```

Code to erase all FLASH memory

```
FLERASE   LDA     #%0000 0110
          STA     $FE08          Set ERASE and MASS bits
          LDA     $FF7E          Read from FLASH block protect
DELAY10   LDX     #$14           10 Microsecond delay
LOOP1 DECX
          BPL     LOOP1          Loop 20 times
          LDA     #%0000 1110
          STA     $FE08          Enable high voltage (HVEN)
DELAY4    LDA     #$10           4 Millisecond delay
LOOP2 NOP
LOOP3 LDX     #$FF
          DECX
          BPL     LOOP3          Loop 255 times
          DECA
          BPL     LOOP2          Loop 16 times
          LDA     #%0000 1100
          STA     $FE08          Clear ERASE  bit
DELAY100  LDA     #$BE           100 Microsecond delay
LOOP4 DECA
          BPL     LOOP4          Loop 190 times
          LDA     #%0000 0000    Disable high voltage
DELAY10   LDX     #$14           10 Microsecond delay
LOOP5 DECX
          BPL     LOOP5          Loop 20 times
          RTS
```

Appendix C: RELATIVE SPECTRAL POWER GRAPHS

Data sheets for each LED contain a graph of the relative radiant power versus the wavelength of light. The following tables show the values read from the spectral power graphs, used to create figures 6.7 and 6.8.

OPE5594A:

Wavelength (nm)	Relative Radiance
900	0.000
905	0.023
910	0.076
915	0.135
920	0.211
925	0.323
930	0.612
935	0.861
940	0.983
945	0.990
950	0.947
955	0.875
960	0.776
965	0.594
970	0.396
975	0.290
980	0.224
985	0.172
990	0.122
995	0.079
1000	0.036
1005	0.007

OPE5685:

Wavelength (nm)	Relative Radiance
800	0.000
805	0.000
810	0.001
815	0.056
820	0.122
825	0.182
830	0.257
835	0.439
840	0.802
845	0.957
850	1.000
855	0.967
860	0.908
865	0.818
870	0.673
875	0.452
880	0.317
885	0.244
890	0.188
895	0.139
900	0.092
905	0.053

TSUS5400:

Wavelength (nm)	Relative Radiance
900	0.110
905	0.131
910	0.178
915	0.259
920	0.367
925	0.515
930	0.689
935	0.830
940	0.936
945	0.981
950	1.000
955	0.988
960	0.950
965	0.839
970	0.675
975	0.522
980	0.392
985	0.306
990	0.241
995	0.196
1000	0.167
1005	0.153

TSHA440:

Wavelength (nm)	Relative Radiance
780	0.015
785	0.027
790	0.047
795	0.074
800	0.106
805	0.144
810	0.191
815	0.242
820	0.304
825	0.363
830	0.441
835	0.527
840	0.625
845	0.722
850	0.808
855	0.875
860	0.924
865	0.962
870	0.990
875	1.000
880	0.984
885	0.948
890	0.896
895	0.830
900	0.752
905	0.668
910	0.583
915	0.497
920	0.424
925	0.357
930	0.289
935	0.226
940	0.174
945	0.127
950	0.088
955	0.064
960	0.046
965	0.032
970	0.017
975	0.008
980	0.003
985	0.000
990	0.000
995	0.000